CASE REPORT

Therapeutic Drug Monitoring in Peritoneal Dialysis: A Case of *Klebsiella pneumoniae* Peritonitis Treated with Gentamicin.

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Abstract

Peritonitis is a common complication of peritoneal dialysis. Prompt initiation of antibiotic therapy is consistently associated with improved outcomes. Antibiotics for peritonitis may be delivered via the intraperitoneal or systemic route. The pharmacokinetics of gentamicin in patients on continuous ambulatory peritoneal dialysis (CAPD) are highly variable, complicating dosing decisions to balance between efficacy and avoid toxicity. The implementation of therapeutic drug monitoring is important in adjusting gentamicin serum concentrations in patients receiving CAPD.

Keywords: *Continuous ambulatory peritoneal dialysis, gentamicin, peritonitis, therapeutic drug monitoring,*

Introduction

Peritonitis is a common complication of peritoneal dialysis [1,2]. Diagnosis of peritoneal dialysis (PD)-related peritonitis is established when at least two of the following criteria are met: (i) clinical features such as abdominal pain or cloudy dialysis effluent; (ii) dialysis effluent white cell count >100/μL (or >0.1 × 10^9/L) after a dwell time of at least two hours with >50% polymorphonuclear leukocytes; or (iii) a positive dialysis effluent culture [2].

Antibiotics for peritonitis may be delivered via the intraperitoneal (IP) or systemic route [2]. Prompt initiation of antibiotic therapy is consistently associated with improved outcomes. The IP route is preferred as it provides high local drug concentrations at the site of infection while minimizing systemic toxicity [3]. Nevertheless, IP-administered drugs can still be absorbed into the systemic circulation, potentially causing adverse effects [2].

Aminoglycosides' efficacy is best described by concentration-dependent killing, with optimal outcomes achieved when the peak serum concentration reaches 8–10 times the minimum inhibitory concentration (MIC), and by an exposure-response relationship characterized by an *area under the curve/MIC (*AUC/MIC) ratio >70 [3]. However, serum aminoglycoside levels do not correlate well with peritonitis outcomes [4]. This may be explained by the limitations of standard microbiological testing, such as MIC determinations, which do not account for the unique circumstances of PD–associated peritonitis, where intraperitoneal antibiotics exert their effect primarily at the local site of infection. The International Society for Peritoneal Dialysis (ISPD) Guidelines recommend that peripheral blood aminoglycoside levels be monitored mainly for the detection of toxicity rather than as a measure of therapeutic efficacy [2].

Although IP administration is preferred, systemic therapy may be required when IP access is not feasible [5]. In such cases, aminoglycoside dosing should follow recommendations for patients with end-stage renal disease receiving hemodialysis. Achieving target serum concentrations is challenging with both intravenous (IV) and IP aminoglycoside dosing in patients undergoing peritoneal dialysis. Hereby, we describe a case of *Klebsiella pneumoniae* peritonitis managed with gentamicin therapy.

Case description

This is a 53-year-old man (weight 58 kg), a known case of chronic kidney disease with CAPD commenced in 2024. On the current admission, he presented with a two-day history of generalized abdominal pain and vomiting, along with 3 days of loose stools (more than seven episodes per day) and cloudy peritoneal dialysis effluent with a white cell count >230 cells/mm^3. Empirical treatment for peritonitis was initiated on the first day of hospitalization with IP ceftazidime and IP cefazolin (1 g stat, followed by 250 mg four times daily). Peritoneal fluid culture was obtained prior to initiation of antibiotics, and by day 3 of admission, gram-negative peritonitis was confirmed by the isolation of *Klebsiella pneumoniae*, which was sensitive to amoxicillin–clavulanate, trimethoprim–sulfamethoxazole, and gentamicin (MIC <1). Based on the culture and sensitivity findings, IP cefazolin was discontinued, and therapy was adjusted to IV ceftazidime 1g once daily and IV gentamicin 120mg single dose. A blocked Tenckhoff catheter, evidenced by poor inflow and outflow on day 3 of admission, necessitated the switch to systemic administration.

Serum gentamicin levels were measured 2 hours after intravenous administration and again on 36 hours post-dose. The concentrations were 6.1 mg/L and 2.9 mg/L, respectively. The calculated peak level was 6.23 mg/L, which was within the

therapeutic range, but the trough level (2.9mg/L) exceeded the recommended target of <1mg/L. Thus, the gentamicin dose was withheld, and a random gentamicin level was re-measured 60 hours after the previous dose, which returned at 2.1 mg/L—slightly above the target range (Figure 1). As the gentamicin level remained above 1 mg/L, the next dose was withheld for an additional day. On Day 4 post gentamicin dose, Tenkoff catheter flushing with urokinase was performed, and CAPD was resumed with four exchanges daily (06:00, 12:00, 18:00, and 22:00). Given the improved inflow and outflow through the Tenkoff catheter, the antibiotic administration route was changed from intravenous to intraperitoneal. IP gentamicin 0.6mg/kg (35 mg) once daily at 18:00 (4-hour dwell time) was initiated on Day 5 of gentamicin together with IP ceftazidime 250mg 4 times a day. A 4-hour dwell time for IP gentamicin was chosen to reduce systemic absorption and allow for consistent daily dosing. Following this fixed dosing regimen, gentamicin trough serum concentrations remained below 2 mg/L, with therapeutic drug monitoring demonstrating levels of 0.9 mg/L on day 7 and <0.5 mg/L on day 9.

Subsequent peritoneal fluid cultures obtained on days 3 and 5 of gentamicin therapy remained negative. No further peritoneal fluid cultures were performed until completion of the 21-day antibiotic course. The peritoneal fluid cell count demonstrated a decreasing trend in total white blood cells, and by day 5 of gentamicin therapy, no white cells were detected in the peritoneal dialysis effluent. The effluent remained clear from the initiation of antibiotic therapy through to completion of the 21-day course. The patient tolerated gentamicin well, with no evidence of drug-related toxicity, particularly ototoxicity.

On day 10 of antibiotic therapy, the patient developed encephalopathy, presenting with confusion and delirium suspected to be due to the cephalosporin antibiotic. Consequently, CAPD and all antibiotics were withheld. A femoral vein cannulation was performed to facilitate the initiation of hemodialysis, which was commenced on the same day. CAPD was resumed on day 12, and the patient was switched to intraperitoneal meropenem to complete a total of 21 days of antibiotic therapy as per the ISPD guideline for gram-negative peritonitis infection.

Discussion

Aminoglycosides such as gentamicin remain valuable for the treatment of Gram-negative peritonitis, including *Klebsiella pneumoniae* infection, because they exhibit concentration-dependent bactericidal activity [1,2]. Maximal bacterial killing occurs at high peak drug concentrations, and aminoglycosides also display a post-antibiotic effect, whereby bacterial growth suppression persists even after drug concentrations fall below the organism's MIC [2]. Owing to this combination of concentration-dependent killing and post-antibiotic effect, intermittent once-daily intraperitoneal dosing is generally preferred to maintain efficacy while reducing adaptive resistance and minimizing toxicity.

In PD patients, reduced renal clearance and increased systemic absorption of gentamicin during peritonitis prolong its plasma elimination half-life and may lead to drug accumulation with an attendant rise in toxicity risk [2]. A major concern with aminoglycoside use in PD patients is ototoxicity, the mechanism of which remains incompletely understood [6,7]. IP administration of antibiotics is generally recommended for PD-related peritonitis because it achieves high peritoneal concentrations at the site of infection; however, serum levels may be subtherapeutic in the setting of severe systemic infection or bacteremia [2]. Conversely, intravenous administration produces higher systemic and tissue concentrations, which is advantageous in cases complicated by sepsis, bacteremia, or deep-seated infection, but only a small fraction of the drug penetrates the peritoneal cavity [3,5].

Current ISPD guidelines therefore favor IP aminoglycoside therapy for peritonitis, reserving IV administration for situations with concurrent severe systemic infection, hemodynamic instability, or when IP therapy is not feasible.

In a study by Farkas et al., the percentage target attainment for indices of treatment success was defined as an IP peak/MIC ratio >10 [3]. It was evaluated for various intraperitoneal gentamicin regimens (0.3–1.2 mg/kg once every 24 hours) across dwell times of 2–6 hours over a 2-week treatment course [3]. All regimens achieved adequate efficacy for organisms with MIC ≤1 mg/L. For organisms with MIC 2 mg/L, only IP doses of ≥0.6 mg/kg reached the desired pharmacokinetic/pharmacodynamic targets. At MIC 4 mg/L, the clinical breakpoint, only the 1.2 mg/kg IP gentamicin regimen consistently achieved the target peak/MIC ratio. Based on these findings, the authors concluded that IP gentamicin 0.6 mg/kg once daily provides an optimal balance in terms of sufficient efficacy for organisms with MIC ≤2 mg/L while minimizing systemic exposure and the risk of toxicity. Current ISPD guidelines therefore recommend intraperitoneal gentamicin at 0.6 mg/kg once daily, administered with a minimum dwell time of 6 hours [2]. Such a recommendation is to ensure sufficient peritoneal exposure while limiting systemic absorption.

Peak gentamicin concentrations of approximately 8–10 × MIC during the first 30–60 minutes are desirable to achieve maximal bactericidal effect [8]. Following intraperitoneal administration, systemic absorption is substantial and was found that by 3 hours about 50% of the dose is absorbed into the circulation, and by the end of the recommended 6-hour dwell time, approximately three-quarters of the total intraperitoneal dose would be absorbed. To preserve the post-antibiotic effect and minimize the risk of toxicity, trough concentrations should remain <2 mg/L. In clinical practice, IP gentamicin doses often need to be withheld for 2 to 3 days due to supratherapeutic trough levels exceeding 2 mg/L, indicating systemic accumulation. Using a shorter dwell time for IP gentamicin than the recommended 6 hours would maintain a similar peak/MIC ratio in the peritoneal dialysate with the benefit of lower systemic absorption, reduced trough plasma concentrations, and a decreased risk of toxicity. This approach may therefore allow more consistent daily dosing without the need to withhold doses. In our case, the use of a 4-hour dwell time with 0.6 mg/kg IP gentamicin resulted in trough levels consistently below 2 mg/L, supporting this concept.

If PD patients develop a systemic infection other than peritonitis, or when intraperitoneal antibiotic administration is not feasible, IV gentamicin should be given using the same approach as in patients with end-stage renal failure. The recommended regimen for adults undergoing hemodialysis consists of gentamicin 1–2 mg/kg, with monitoring of both peak and trough serum concentrations [9,10].

Conclusion

This case report highlights that, regardless of the dosing strategy employed, appropriate monitoring of serum gentamicin levels is essential to achieve maximal efficacy for both intravenous and intraperitoneal administration in patients undergoing CAPD. Trough concentrations should remain <2 mg/L to avoid prolonged supratherapeutic exposure. Achieving therapeutic peak and trough levels maximizes antibacterial efficacy while minimizing the risks of toxicity [7-11]. In this case, a shortened dwell time of 4 hours appeared to reduce systemic absorption while maintaining desirable trough concentrations, highlighting a potential dosing approach that deserves further evaluation.

Consent: Verbal informed consent was obtained from the patient for publication of this case report.

Conflict of Interest
The authors have no funding or conflicts of interest to disclose. The first author is currently undergoing training under the Malaysia Advanced Clinical Pharmacy Programme (MyACPP - Clinical Pharmacokinetic).

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Authors' Contribution
KLSF performed the literature search and manuscript preparation while SM was responsible for critical revision of the manuscript for intellectual content. All authors agreed and approved the manuscript for publication.

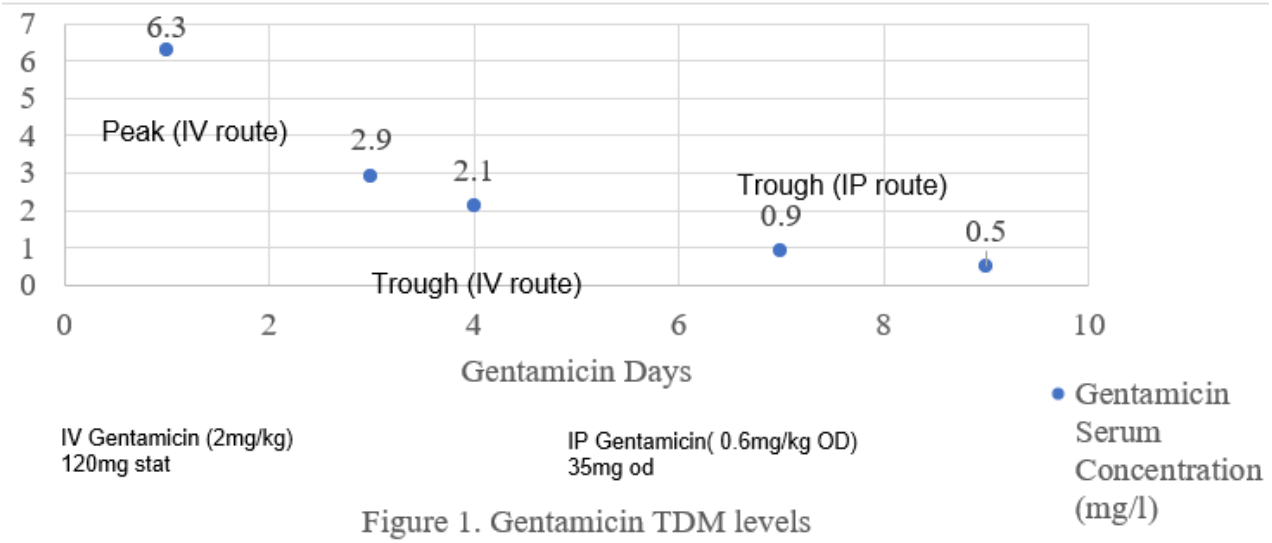

Figure 1. Gentamicin TDM levels

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