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Use of high doses of intraperitoneal amikacin to preserve the peritoneal catheter during *Pseudomonas aeruginosa* peritonitis

(Utilisation des hautes doses d'amikacine intrapéritoneale pour la sauvegarde du cathéter péritonéal au cours d'une péritonite à Pseudomonas Aeruginosa)

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Summary

This article reports a clinical case illustrating the use of high-dose intraperitoneal amikacin to preserve the peritoneal catheter in a patient with *Pseudomonas aeruginosa* peritonitis undergoing chronic peritoneal dialysis. *Pseudomonas peritonitis* is known for its severity, poor response to standard treatments, and high probability of leading to catheter removal, often resulting in a harmful transition to hemodialysis.

The patient, aged 46, with stage V renal failure secondary to HIV-associated nephropathy, had been treated with continuous ambulatory peritoneal dialysis since 2021. After an episode of Pseudomonas peritonitis in 2023, which was successfully treated, he presented in 2024 with a recurrence associated with an infection at the catheter exit site. Despite empirical and then targeted antibiotic therapy in accordance with ISPD recommendations (cephalosporin, gentamicin, then cefepime and ciprofloxacin, then meropenem instead of cefepime), the biological progression remained unfavorable, with persistently high cellularity in the peritoneal fluid.

Given this lack of response, high-dose intraperitoneal amikacin bolusesup to 12 mg/kg) were administered. Each injection was followed by a marked decrease in peritoneal cellularity, although there was an initial rebound requiring repeated administrations. After a third and final lower dose, complete normalization of the dialysis fluid was achieved without removal of the catheter.

No adverse effects, particularly auditory or vestibular, were observed in the short or medium term, although no systematic audiometry was performed at a distance. The authors emphasize the pharmacodynamic interest of intraperitoneal administration, which enables high local concentrations well above the MIC while limiting systemic exposure.

In conclusion, this case suggests that the exceptional use of high intraperitoneal doses of amikacin may represent an effective rescue option in selected patients, when catheter removal is associated with a high risk of morbidity and mortality.

Keywords: peritoneal dialysis, peritonitis, amikacin, vestibular toxicity, auditory toxicity

Résumé

Cet article rapporte un cas clinique illustrant l'utilisation de hautes doses d'amikacine par voie intrapéritonéale comme stratégie de sauvetage du cathéter péritonéal chez un patient atteint d'une péritonite à *Pseudomonas aeruginosa* en dialyse péritonéale chronique. Les péritonites à *Pseudomonas* sont connues pour leur gravité, leur mauvaise réponse aux traitements standards et leur forte probabilité d'aboutir à l'ablation du cathéter, avec un passage souvent délétère en hémodialyse.

Le patient, âgé de 46 ans, insuffisant rénal stade V secondaire à une néphropathie associée au VIH, était traité par dialyse péritonéale continue ambulatoire depuis 2021. Après un premier épisode de péritonite à *Pseudomonas* correctement traité en 2023, il a présenté en 2024 une récidive associée à une infection du site de sortie du cathéter. Malgré une antibiothérapie empirique puis ciblée conforme aux recommandations de l'ISPD (céphalosporine, gentamicine, puis céfépime et ciprofloxacine, puis méropénème au lieu du céfépime), l'évolution biologique est restée défavorable, avec une persistance élevée de la cellularité du liquide péritonéal.

Face à cette absence de réponse, des bolus intrapéritonéaux d'amikacine à fortes doses (jusqu'à 12 mg/kg) ont été administrés. Chaque injection a été suivie d'une chute marquée de la cellularité péritonéale, avec toutefois un rebond initial nécessitant des administrations répétées. Après une troisième et dernière dose plus faible, une normalisation complète du liquide de dialyse a été obtenue, sans retrait du cathéter.

Aucun effet indésirable, notamment auditif ou vestibulaire, n'a été observé à court ou moyen terme, bien qu'aucune audiométrie systématique n'ait été réalisée à distance. Les auteurs soulignent l'intérêt pharmacodynamique de l'administration intrapéritonéale, qui permet d'atteindre des concentrations locales élevées, largement supérieures à la CMI, tout en limitant l'exposition systémique.

En conclusion, ce cas suggère que l'utilisation exceptionnelle de hautes doses intrapéritonéales d'amikacine peut représenter une option de sauvetage efficace chez des patients sélectionnés, lorsque l'ablation du cathéter est associée à un risque élevé de morbidité et de mortalité.

Mots-clés : dialyse péritonéale, péritonite, amikacine, toxicité vestibulaire, toxicité auditive

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Introduction

Pseudomonas peritonitis in chronic peritoneal dialysis (PD) is often difficult to treat and sometimes leads to catheter removal and either temporary or permanent suspension of PD.

It is often accompanied by a simultaneous infection at the catheter exit site, caused by the same microorganism.

The presence of biofilm has been reported as a major cause of non-response to antibiotics and necessitates a much higher concentration than the MIC (in fact, we would refer to an MIC for biofilm) [1].

In the event of a lack of response, discontinuing PD complicates the patient's progress, requiring transfer to hemodialysis (HD), which increases costs, morbidity, and mortality.
The use of high intraperitoneal doses of amikacin (7.5 to 15 mg/kg) has already been reported in the literature in isolated cases [2]. In fact, a study on the use of aminoglycosides used simulation to show the concentrations reached in the intraperitoneal and systemic spaces [3].

However, the risk of adverse effects on the vestibular region and hearing has also been established. Recently, ISPD recommendations have included preventive treatment with N-acetylcysteine to minimize or even prevent this ototoxicity [4, 5].

Amikacin, like other aminoglycosides, is effective when its maximum serum or intraperitoneal concentration is 8–20 times higher than the MIC. It is advisable to maintain this concentration for at least 1 to 2 hours to ensure a good response to the drug. After this period, it is essential to reduce the serum concentration to avoid or reduce ototoxicity [6, 2].

This can be achieved in cases of chronic PD by using a cycler (DPA) or by performing an HD session if the patient has vascular access. It is imperative to measure the serum concentration of amikacin to ensure this reduction.

Observation

The patient was a 46-year-old man who had been suffering from end-stage renal failure since December 2021 due to HIV-related nephropathy. He was prescribed CAPD treatment at a rate of two bags per day, which was possible due to residual diuresis of two liters of urine per day.

The first year of treatment was well tolerated, but then an episode of peritonitis occurred.

Bacteriological examination revealed the presence of *Pseudomonas aeruginosa*. Empirical treatment was successfully instituted on an outpatient basis and, once cultures were completed, replaced by targeted antibiotic therapy in accordance with the 2016 ISPD recommendations (updated in 2022).

In December 2023, extrusion of the superficial Dacron cuff was observed and treated by shaving.

In May 2024, after complaining of watery diarrhea for several days, the patient presented to the

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PD center with abdominal pain, nausea, and cloudy PD fluid. The catheter exit site, where the superficial Dacron sleeve had been shaved, was oozing fluid that was spreading onto the dressing. On the third day, a swab of the exit site revealed the presence of Pseudomonas. Due to his satisfactory clinical condition, the decision was made to treat the patient on an outpatient basis.

Initial laboratory data on the PD fluid showed a total cell count of 50,039/mm^3, with 85% neutrophils and 12% monocytes. Empirical treatment (cephalosporin and gentamicin) in accordance with ISPD recommendations was initiated. Forty-eight hours after a positive culture for *Pseudomonas aeruginosa* (antibiogram with sensitivity for cefepime MIC = 2 mg/L, ciprofloxacin MIC = 0.25 mg/L, and meropenem MIC = 0.5 mg/L), treatment was changed to cefepime 2 g per day, with prolonged contact time (more than 6 hours), and ciprofloxacin 500 mg orally twice a day. Despite this targeted treatment, the total cell count in the peritoneal fluid remained at 4,893 on the seventh day.

A dose of 1 g of amikacin (12 mg/kg) was then injected intraperitoneally. An initial favorable response was observed, with a decrease in cell count to 498/mm3, but this was followed by a rebound in cell count over the following days, reaching over 4,000/mm3. A second dose of 1 g of amikacin was administered intraperitoneally, followed by a second significant decrease in cell count (see graph). On day 15, cefepime was changed to meropenem. This change was followed by a reduction in cell count, reaching a plateau of approximately 370 cells/mm3. Finally, on day 20, a third dose of 500 mg (5 mg/kg) of amikacin was administered, after which the total cell count normalized *(Figure 1)*. No side effects were observed in the short term (one month later), and the patient resumed work as normal. Two years have subsequently passed, and the patient has reported no signs of ototoxicity. However, no audiogram was performed after the first year.

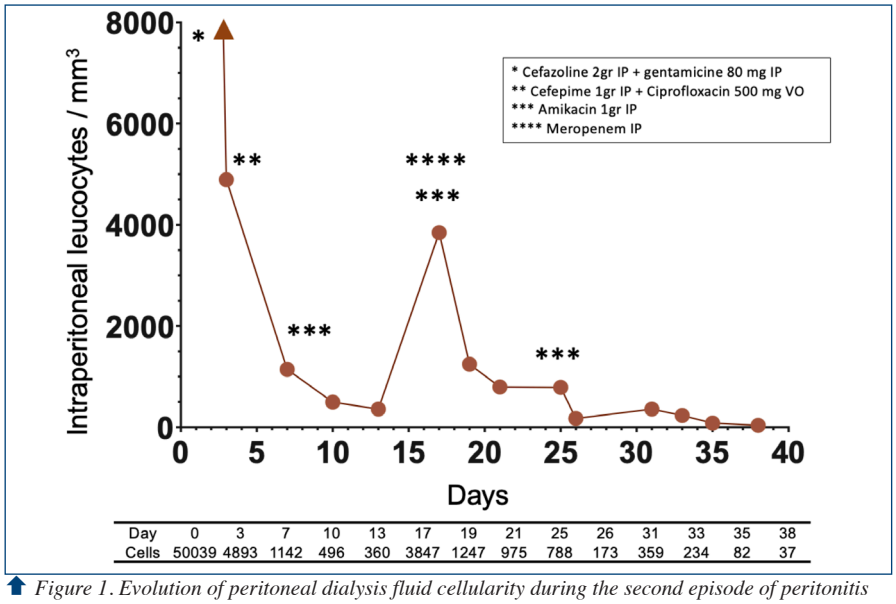

Figure 1. Evolution of peritoneal dialysis fluid cellularity during the second episode of peritonitis

Discussion

Pseudomonas aeruginosa peritonitis following infection of the catheter exit site is difficult to treat and often results in catheter removal. According to the ÍSPD, treatment should include two long-term medications (21 days each). Antibiotic resistance (multidrug resistance or MDR) may

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occur, resulting in a cure rate of less than 50% [1].

For aminoglycosides such as amikacin, achieving peak serum concentrations above the MIC is essential for a positive response to infection. In this clinical case, amikacin provided effective treatment for *Pseudomonas aeruginosa* peritonitis that had not responded to ISPD standards of care. In addition, the catheter was not removed at the end of the fifth day, despite ISPD recommendations, because the patient was clinically stable.

The use of high intraperitoneal amikacin doses was followed by a sharp drop in cell count. The intraperitoneal concentration of amikacin administered IP can reach a level 10 times the MIC [2,7], without being accompanied by a similarly high serum concentration, which minimizes other toxic effects (nephrotoxicity and ototoxicity).

We did not use a cycler or hemodialysis after amikacin infusions. However, this would be highly desirable, as it is a low protein-binding antibiotic (approximately 10%) and a significant amount (approximately 20%) of the drug can be dialyzed.

Conclusion

This modality (emergency treatment) with 1–3 high intraperitoneal doses (7.5-15 mg/kg) of amikacin should be considered in exceptional cases in which removal of the peritoneal catheter may be complicated by increased morbidity and mortality.

Authors' Contributions

Javier de Arteaga designed and wrote the article. Fabian Ledesma and Graciela Gonzales (PD nurses) created the graph. Pehuen Fernandez, Carlos Chiurchiu Walter Douthat, and Jorge de la Fuente proofread the article and provided constructive comments for its revision.

Ethical Considerations and Patient Consent

The patient was informed of the plan to publish his case after complete anonymization and provided verbal consent.

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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Data availability

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