Treatment with intravenous daptomycin for a peritonitis relapse caused by *Staphylococcus epidermidis*

Nefrologia 2011;31(3):374-5
doi:10.3265/Nefrologia.pre2011.Mar.10810

To the Editor,

Peritonitis is one of the main complications for patients on kidney replacement therapy with peritoneal dialysis. In many cases, peritonitis causes the technique to fail, meaning that the patient has to be transferred to haemodialysis.[1,2]

We present here the case of a patient with two relapses caused by the same germ, probably caused by the colonisation of the catheter, who responded well to treatment with intravenous daptomycin.

The patient was a 79-year-old male with stage 5 chronic kidney disease secondary to nephroangiosclerosis and/or diabetic nephropathy, who was on kidney replacement therapy with continuous ambulatory peritoneal dialysis. The patient also had long-term type-2 diabetes mellitus, arterial hypertension and pernicious anaemia.

The patient came to the emergency department 27 months after starting treatment with symptoms and a cell count in the drainage fluid compatible with peritonitis. The empiric protocol established in our department which includes vancomycin and ceftazidime was started and cultures were also taken.

Staphylococcus epidermidis grew in the peritoneal fluid in the following days. The treatment with ceftazidime was stopped and intraperitoneal vancomycin was continued on an ambulatory basis until the treatment had been followed for 15 days.

The patient once again had abdominal pain and cloudy fluid 7 after finishing the treatment. New cultures were taken and the empiric treatment was restarted, but this time it was accompanied with prophylactic antifungal treatment. *S. epidermidis* grew once again in the cultures with a similar antibiogram to the one seen during the first episode and with a similar minimum inhibitory concentration (MIC) for vancomycin to the previous one (2μg/ml). Given the growth of the same germ and the short time period between the end of treatment and the new episode, it was considered as a relapse and antibiotic treatment was indicated for three weeks with intraperitoneal vancomycin plus oral rifampicin. An ultrasound of the abdomen and the catheter tunnel was requested at that time in order to rule out intraperitoneal fluid collections or collections in the pathway of the catheter.

The patient had a new episode with exactly the same germ once the antibiotic treatment had been completed. The need to transfer the patient to haemodialysis was considered at this point in order to take out the catheter as colonisation was suspected. As vascular access was difficult, we decided to try treatment with intravenous daptomycin at a dose of 4mg/kg/48h for 10 days.

At present, four months after ending treatment, the patient has not had any new episodes. He has been able to continue with his dialysis treatment and we were able to avoid removing the peritoneal catheter.

Peritonitis relapse is defined as a new episode of peritonitis with the same result in the culture within four weeks of completing treatment. It is usually associated with resistance to antibiotics and a biofilm presence on the catheter. Studies have been published that report the need to increase the dose or use multiple antibiotics to eradicate the germ. In the case of *S. epidermidis*, it is recommended that treatment is continued for at least 21 days.[3-6]

There is little information in the medical literature which evaluates treatment with daptomycin in peritoneal dialysis by intravenous or intraperitoneal route. In our case, daptomycin was probably able to enter inside the biofilm on the catheter and eradicate the germ that was causing the peritonitis and the subsequent relapses.

Although clinical studies are obviously needed to determine how valid this therapeutic option is, it was very useful in our case as the patient did not have to have the catheter removed.

As a result, intravenous daptomycin is an option that must be taken into account when it is suspected that the catheter has been contaminated by *S. epidermidis* in patients with peritonitis on peritoneal dialysis.

1. Woodrow G, Turney JH, Brownjohn AM. Technique failure in peritoneal dialysis and its impact on patient survival. Perit Dial Int 1997;17:360.
2. Holley HL, Piraino BM. Complications of peritoneal dialysis: diagnosis and management. Semin Dial 1990;3:245.
3. Dasgupta MK, Kowalewaska-Grochowska K, Costerton JW. Biofilm and peritonitis in peritoneal dialysis. Perit Dial Int 1993;13(Suppl 2):S322.
4. Piraino B, Bailie GR, Bernardini J, Boeschoten E, Gupta A, Holmes C, et al. Peritoneal dialysis-related infections recommendations: 2005 update. Perit Dial Int 2005;25:107.
5. Anwar H, Dasgupta MK, Costerton JW. Testing the susceptibility of bacteria in biofilms to antibacterial agents. Antimicrob Agents Chemother 1990;34:2043.
6. Finkelstein ES, Jekel J, Troidle L, Gorban-Brennan N, Finkelstein FO, Bia FJ. Patterns of infection in patients maintained on long-term peritoneal dialysis therapy with multiple episodes of peritonitis. Am J Kidney Dis 2002;39:1278.
7. Goedecke VA, Clajus C, Burkhard O. Pharmacokinetics and dialysate levels of daptomycin given intravenously in peritoneal dialysis patient. Scan J Infect Dis 2009;41:155-7.

8. Hermsen ED, Hovde LB, Hotchkiss JR, Rotschafer JC. Increased killing of staphylococci and streptococci by daptomycin compared whit cefazolin and vancomycin in an in vitro peritoneal dialysate model. Antimicrob Agents Chemother 2003;47:3764-7.

F. Levy[1], V. Camarero Temiño[1], A. Blasco Mollá[2], M.P. Ortega Lafont[2], P. Abaigar Luquin[1], M.J. Izquierdo Ortiz[1], G. Torres Torres[1]

[1] Nephrology Department.
Healthcare Complex of Burgos, Spain
[2] Microbiology Department.
Healthcare Complex of Burgos, Spain
Correspondence: F. Levy
Servicio de Nefrología.
Complejo Universitario Asistencial de Burgos.
federicolevy@yahoo.com.ar

Intraperitoneal daptomycin

Nefrologia 2011;31(3):375-6
doi:10.3265/Nefrologia.pre2011.Mar.10806

To the Editor,

Peritonitis is one of the main causes of morbidity in patients undergoing peritoneal dialysis (PD). Although the usual treatments with vancomycin, aminoglycosides or semi-synthetic penicillins recommended in treatment guidelines for peritonitis[1] are efficient in most cases, situations such as colonisation by methicillin-resistant microorganisms with some degree of resistance to vancomycin are common. These treatments are ineffective in these cases.

The proliferation of multi-resistant gram-positive pathogens has led to the antibiotic daptomycin being brought back and its clinical development has started again. It was approved by the United States Food and Drug Administration (FDA) in 2003 for the treatment of endocarditis caused by gram-positive pathogens, and skin and white-tissue infections.

A case study has been published of peritonitis which was not linked to the peritoneal catheter that was treated with intravenous daptomycin. This study analysed the concentration of daptomycin reached in the peritoneal fluid after intravenous administration. It was found to be 5mg/ml (minimum inhibitory concentration [MIC]=4mg/ml).[2] Therefore, the concentrations in the intraperitoneal fluid as a result of intraperitoneal administration of the antibiotic would be less close to the microorganism MIC for daptomycin.

The clinical experience published to date is limited to two cases. Intraperitoneal daptomycin was used in these cases to treat peritonitis caused by vancomycin-resistant gram-positive bacteria.[3] This treatment succeeded in these cases where conventional therapies had previously failed. The intraperitoneal administration of daptomycin was well tolerated in these patients and they had no peritoneal irritation or negative effects associated with the administration of drugs through this route.

Furthermore, daptomycin is a drug that is currently used to treat catheter-related bacteriaemias[4] due to its efficacy in controlling biofilm growth, and that is why it may be considered useful in the treatment of biofilm on intraperitoneal catheters.

We report here the clinical case of a 61-year-old man who had been diagnosed with advanced chronic kidney disease (CKD) secondary to diabetic nephropathy since 2001. He started PD in December 2006. The patient has had three episodes of peritonitis since February 2008 that led us to consider removing the catheter in October 2009 due to suspected biofilm.

In May 2010 he had a new episode of peritonitis and was started on intraperitoneal empiric treatment with vancomycin following normal dosage guidelines (a shock dosage of 2g followed by 2g/3 days and a shock dosage of 100mg of tobramycin and 50mg/24h). The presence of *Staphylococcus epidermidis* and *Streptococcus viridans* which were only sensitive to carbapenems was found four days later when the culture results were received. We, therefore, continued with the intraperitoneal treatment with vancomycin at a dose of 2g a week (3 weeks), and tobramycin was changed for 1g of imipenem/24h for 14 days.

He had a new relapse in June 2010 and *S. epidermidis* with intermediate sensitivity to vancomycin (MIC=2) was isolated. Treatment with vancomycin was started according to protocol, with a positive clinical response, although after this relapse, it was suspected that the peritoneal catheter had been colonised by *S. epidermidis* biofilm. An application was made for the compassionate use of intraperitoneal daptomycin on the basis of the previous experience of two clinical cases published. Treatment with vancomycin was maintained until daptomycin was authorised.

We used the following treatment plan with daptomycin:

A shock dosage of 200mg (in a 2l PD1 solution), followed by 40mg in each change of the intraperitoneal fluid (four times a day) for 10 days. After finishing this treatment plan, the catheter was then put in an antibiotic lock with 350mg in 7ml for 12h once a week for one month. The patient responded positively to this treatment and has had no relapses or new episodes of peritonitis.

1. Furgeson SB, Teiltelbaum I. New treatment options and protocols for peritoneal dialysis-related peritonitis. Contrib Nephrol 2009;163:169-76.
2. Burklein D, Heyn J, Kirchhoff C, Ozimek A, Traunmuller F, Joukhadar C, et al. Analysis of plasma and peritoneal fluid concentrations of daptomycin in a patient with *Enterococcus faecium peritonitis*. Int J Antimicrob Agents 2008;32(4):369-71.
3. Huem SC, Hall I, Topal J, Mahnenmith R, Brewster U, Abu-alfa A. Successful use of intraperitoneal daptomicyn in the treatment of vancomycin-resistant enterococcus peritonitis. Am J Kidney Dis 2009;54(3):538-41.
4. Raad I, Hanna H, Jiang Y, Dvorak T, Reitzel R, Chaiban G, et al. Comparative activities