

Daptomycin in peritoneal dialysis, intraperitoneal or intravenous[☆]

Daptomicina en diálisis peritoneal, intraperitoneal o intravenosa

Dear Editor,

Recurrent peritonitis due to a suspected biofilm causes substantial morbidity in patients with peritoneal dialysis (PD) and sometimes leads to permanent abandonment of the technique.

We present the case of a 55-year-old man with a prior history of meningitis due to listeria, resolved with antibiotic treatment, chronic kidney disease (CKD) secondary to membranous glomerulonephritis in PD and an adrenal incidentaloma.

He visited our department owing to signs and symptoms of peritonitis due to clinically asymptomatic *Staphylococcus epidermidis*, which resolved with intraperitoneal (IP) vancomycin administered for 14 days. The post-treatment monitoring culture was negative.

Fifteen days after completion of antibiotic therapy, he had a recurrence of peritonitis caused by the same microorganism, and then he was treated with oral ciprofloxacin adjusted to antibiogram results without achieving a negative peritoneal fluid culture. Given the suspicion of recurring peritonitis due to a biofilm, intravenous (IV) daptomycin was started at a dose of 500 mg/48 h (residual diuresis 400 ml/24 h). After 10 days of treatment, the fluid remained slightly cloudy (220 cells/ μ l, 55% polymorphonuclear cells, 45% monomorphonuclear cells), with a positive culture for *S. epidermidis*. Therefore, treatment was started with IP daptomycin (200 mg loading dose followed by 40 mg in each exchange) and maintained for 14 days. Throughout this time, the patient received associated antifungal prophylaxis.

The peritoneal fluid culture during and after treatment was negative.

After completing intraperitoneal antibiotic treatment, the patient resumed his usual therapy (automatic PD with a daytime exchange). He was scheduled for daptomycin lseal therapy, administered once per week for 4 weeks.

The sealing therapy protocol was performed using 35 mg of daptomycin in 7 ml of lactated Ringer's solution, with the abdomen empty for a minimum of 12 h.

Currently, the patient remains asymptomatic, and has had no more episodes of peritonitis.

Daptomycin is a lipopeptide antibiotic indicated in the treatment of bacteraemia, right-sided endocarditis and complicated skin infections, with anti-biofilm activity.¹

Several cases of treatment of peritonitis in PD with both IV and IP daptomycin have been reported.

Goedecke et al. showed that intravenous administration of daptomycin achieved plasma and peritoneal fluid levels greater than the minimum inhibitory concentration for microorganisms sensitive to this antibiotic. However, the study was conducted in a single patient.²

Subsequently, several cases were reported of peritonitis in PD that were successfully treated with IV daptomycin.^{3,4}

A study of the pharmacokinetics of daptomycin in PD, with the dual aim of evaluating the drug's penetration of the peritoneal cavity and obtaining a dose regimen to be administered in this type of patients that offered safety and prevented toxicity, concluded that administration at doses of 4–6 mg/kg/48 h is an appropriate regimen for treating non-peritoneal systemic infections in patients who receive continuous ambulatory PD but, owing to its limited penetration of the abdominal cavity, its administration by the IV route is not safe for the treatment of peritonitis.⁵

In the case presented, daptomycin administered by the intravenous route did not achieve a negative peritoneal fluid culture. At the time of administration, peritoneal inflammation was not substantial, and the percentage of polymorphonuclear cells was only 55%, given that the patient was undergoing antibiotic treatment with ciprofloxacin, and the even lower penetration in the abdominal cavity could be attributed to this. Although there have been no studies on how peritoneal inflammation influences the concentration of daptomycin in the peritoneum, a study by Cardone et al.⁵ suggested that the peritoneal inflammation that occurs in the patients studied should to a certain extent promote the drug's penetration of the peritoneal cavity, without being able to ensure whether suitable levels would be achieved as the inflammatory process decreases.

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DOI of original article:

<http://dx.doi.org/10.1016/j.nefro.2015.11.001>.

[☆] Please cite this article as: Pérez Melón C, Borrajo Prol M, Iglesias E, Ferreiro B, Camba Caride M. Daptomicina en diálisis peritoneal, intraperitoneal o intravenosa. *Nefrología.* 2016;36:461–462.

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<http://dx.doi.org/10.1016/j.nefro.2016.09.004>

Treatment of the testosterone deficiency in hemodialysis patients. Preliminary results[☆]

Tratamiento de la deficiencia androgénica del enfermo dializado con suplementos de testosterona. Resultados preliminares

Dear Editor:

Androgen deficiency is an endocrine abnormality that is common in male patients with chronic kidney disease and affects 50%–75% of patients treated with haemodialysis.^{1,2} Its clinical significance is not well known, although various cross-sectional studies have linked low testosterone levels to sexual dysfunction, anaemia, loss of muscle mass, increase in cardiovascular risk and greater mortality.²⁻⁵

Androgens in pharmacological doses have effects on anaemia and nutritional parameters in patients treated with regular haemodialysis.⁶ However, few studies have analysed the effect of treating hypogonadism from renal failure with physiological doses of testosterone, and their results have been controversial.^{7,8}

In this study we present the preliminary data for the results obtained following correction of androgen deficiency in patients treated with haemodialysis.

We defined androgen deficiency as a total serum testosterone concentration lower than 300 ng/dl and an unbound testosterone concentration lower than 225 pMol/l. Testosterone circulates in plasma bound to proteins (especially albumin and a transport globulin [sex hormone-binding globulin, or SHBG]); only 1%–3% circulates unbound. A uraemic patient may have an abnormal SHBG concentration.⁹ Therefore, in patients with chronic kidney disease it is advisable to confirm testosterone deficiency by determining the concentration of unbound testosterone, especially in cases with a total testosterone level that is low but close to the lower limit of the normal range. Unbound testosterone was calculated based on levels of total testosterone, SHBG and albumin.¹⁰

The study was conducted in male patients treated with regular haemodialysis for more than 6 months who were in a stable clinical situation and had not required admission in the last 3 months. All draws for laboratory testing were performed immediately before the first haemodialysis session of the week.

Of the 39 patients analysed, 20 (51%) had a total testosterone concentration lower than 300 ng/dl, all had an unbound testosterone concentration lower than 225 pMol/l, and all were diagnosed with androgen deficiency. Twelve of these 20 patients agreed to participate in the study and granted their written consent. Patients were randomly assigned to the treatment group (6 patients who received testosterone by the transdermal route: one sachet of 5 g of gel containing 50 mg of testosterone daily for 3 months) or the control group (the other 6 patients). The dose of testosterone administered to the treatment group was the minimum initial dose recommended in the medicine's summary of product characteristics.

Patients in the treatment group had a younger age (67 ± 4 vs 75 ± 9 years; $p=0.182$), and at baseline there were no differences between the two groups in terms of the other parameters analysed. [Table 1](#) shows the changes in these parameters. The unbound and total serum testosterone concentration increased in all patients treated, but it only reached the normal range in 4 ([Fig. 1](#)). Neither of the 2 groups of patients showed a change in concentrations of total cholesterol, HDL cholesterol, LDL cholesterol or triglycerides (data not shown).

The prevalence of androgen deficiency in male patients from the haemodialysis unit was 51%. This figure was similar to that observed in other studies. Transdermal administration of testosterone, in the minimum dose recommended in

[☆] Please cite this article as: Pampa Saico S, Teruel Briones JL, Fernández Lucas M, Delgado Yagüe M, García Cano AM, Liaño García F. Tratamiento de la deficiencia androgénica del enfermo dializado con suplementos de testosterona. Resultados preliminares. *Nefrologia*. 2016;36:462-463.