Concentrations were 109.7 and 122.3 hours after the start of haemodialysis, arterial and venous after the three haemodialysis sessions, respectively. Two 154.0 and 195.8 202.2 m


using a F60 polyacrylonitrile dialyser (surface area 1.6 m²) start of haemodialysis. Haemodialysis was performed for 4 h blood samples were performed simultaneously 2 h after the during and after dialysis sessions. Paired arterial and venous blood samples were collected over the dosing interval, before, treatment, in a pharmacokinetic study over 2 weeks.

Serum concentrations were determined after 6 months of 2 weeks for a 23-year-old patient with mRCC. Bevacizumab serum and dialysate concentrations were 500 ml/min and a blood flow rate of 250–300 ml/min. arteriovenous fistula with a constant dialysate flow rate of every 14 days (Table 1).

Subjects with normal renal function [2] receiving 10 mg/kg twice monthly, his bevacizumab area under the curve (AUC) was twice lower than published values (45205 97488 m

The bevacizumab pharmacokinetic parameters of our haemodialysed patient was therefore similar to the reference values reported in patients with normal renal function and, because he was treated by a dose of 5 mg/kg/14days instead of 10 mg/kg twice monthly, his bevacizumab area under the curve (AUC) was twice lower than published values (45205 vs 97488 m h/ml, respectively). Despite a two times lower AUC, the patient had bevacizumab concentrations above the 50% of maximum bevacizumab-induced inhibition (IC50, 104.1 m/ml) during the first 10 days following the infusion.

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Sir, Bevacizumab, a recombinant humanized monoclonal antibody against VEGF (ruMAb VEGF, Avastin®, Genentech, South San Francisco, CA), was approved as a treatment for metastatic renal cell carcinoma (RCC) [1]. However, no bevacizumab pharmacokinetic data are available for patients with renal failure. We report a pharmacokinetic study of bevacizumab in a patient with renal insufficiency requiring haemodialysis.

Bevacizumab was instituted at a dose of 5 mg/kg every 2 weeks for a 23-year-old patient with mRCC. Bevacizumab serum concentrations were determined after 6 months of treatment, in a pharmacokinetic study over 2 weeks.

Blood samples were collected just before and 5, 15, 30 min, and 1, 6, 12 and 24h after the end of infusion. Additional blood samples were collected over the dosing interval, before, during and after dialysis sessions. Paired arterial and venous blood samples were performed simultaneously 2h after the start of haemodialysis. Haemodialysis was performed for 4h using a F60 polyacrylonitrile dialyser (surface area 1.6 m²) every 2 days with a double-needle access to a radial arteriovenous fistula with a constant dialysate flow rate of 500 ml/min and a blood flow rate of 250–300 ml/min.

Bevacizumab serum and dialysate concentrations were measured using an ELISA technique. Bevacizumab pharmacokinetics were analysed by both a non-parametric and a compartmental approach using WinNonLin software (Pharsight Corporation). Pharmacokinetic parameters obtained for our patient were compared with those of subjects with normal renal function [2] receiving 10 mg/kg every 14 days (Table 1).

Bevacizumab concentrations were 90.5 and 125.1 µg/ml; 154.0 and 195.8 µg/ml; and 145.0 and 173.0 µg/ml before and after the third haemodialysis sessions, respectively. Two hours after the start of haemodialysis, arterial and venous concentrations were 109.7 and 122.3 µg/ml; 146.4 and 202.2 µg/ml, and 145.0 and 175.0 µg/ml, respectively. Values of E and CL_{HD} of bevacizumab were 0% and 0 ml/min, respectively. F_{HD} was 0%, i.e. well below the 25% limit value above which haemodialysis clearance should be considered clinically significant.

Since his pharmacokinetic parameters were equivalent to those of patients with normal renal function, we think that the dose of 5 mg/kg would be adapted to the haemodialysed patient. Furthermore, bevacizumab seems not to be dialysable and administration may, thus, be performed anytime before or after the session on haemodialysis days.

Our patient (off-dialysis day) Reference values at steady state in patient with normal renal function

Dose (mg) 5 mg/kg IV 10 mg/kg IV

Dosing interval (day) 14 14

Pharmacokinetics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Our patient</th>
<th>Reference values</th>
</tr>
</thead>
<tbody>
<tr>
<td>c_{max} (µg/ml)</td>
<td>206</td>
<td>284</td>
</tr>
<tr>
<td>c_{min} (µg/ml)</td>
<td>80</td>
<td>NA</td>
</tr>
<tr>
<td>AUC (ng/h/ml)</td>
<td>45205</td>
<td>97488</td>
</tr>
<tr>
<td>T_{1/2} (days)</td>
<td>11.9</td>
<td>20 (11–50)</td>
</tr>
<tr>
<td>CL/F (ml/min)</td>
<td>0.122</td>
<td>0.160</td>
</tr>
<tr>
<td>V_d (l)</td>
<td>2.52</td>
<td>3.25</td>
</tr>
</tbody>
</table>

Haemodialysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Our patient</th>
<th>Reference values</th>
</tr>
</thead>
<tbody>
<tr>
<td>E (%)</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>CL_{HD} (ml/min)</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>F_{HD} (%)</td>
<td>0</td>
<td>NA</td>
</tr>
</tbody>
</table>

\[ C_{H_D} \text{HD: haemodialysis clearance: } \left[ \frac{(\text{Ca} - \text{CV}) \times \text{Qb}}{\text{Ca}} \right] \text{; Ca: concentration entering the dialyser (ng/ml); CV: concentration leaving the dialyser (ng/ml); Qb: blood flow (ml/min); E: extraction coefficient (%)}; \text{CL}_{HD} \text{Qb}; \text{F}_{HD} \text{ (%)}; \text{CL}_{HD}[\text{CL}_{HD} + \text{CL}_{\text{totNHDD}}] \times 100; \text{CL}_{\text{totNHDD}}: \text{total body clearance of the drug on a nonhaemodialysis day (NHDD); NA: not available.}\]


Pancreatitis and pancreatic abscess in a CAPD patient with severe malnutrition

Sir, Previous reports have suggested protein-energy malnutrition as a cause for pancreatitis [1,2]. However, pancreatitis or pancreatic abscesses associated with malnutrition in patients
undergoing continuous ambulatory peritoneal dialysis (CAPD) has not been reported. Furthermore, reports of pancreatic abscess complications in CAPD patients are rare [3]. We report here a CAPD patient who developed severe malnutrition due to depressive disorder, and further developed acute pancreatitis that resulted in widespread intra-abdominal pancreatic abscesses.

A 20-year-old woman was admitted to our hospital for the restoration of her nutritional status. She had been undergoing CAPD since she was 12 years of age, because of congenital bilateral hypoplastic kidney, and was suffering depressive status and concurrent severe malnutrition since the age of 15. She consulted a psychiatrist and was diagnosed with anorexia due to depressive disorder. On admission, her body weight had decreased to 21 kg with a body mass index of 11 kg/m². Gavages of nutritional supplements were started. However, 2 weeks later, she abruptly developed acute pancreatitis. Despite conservative treatments, large pancreatic pseudocysts were noted on computed tomography (CT) 2 months later. Six months after the onset of pancreatitis, she became feverish with increased leucocyte counts in the dialysate. Methicillin-resistant *Staphylococcus epidermidis* was isolated from cultures of blood and intravenous catheter; however, culture of the dialysate was negative. CAPD was stopped and changed to haemodialysis. Ga scintigraphy and contrast-enhanced CT suggested the existence of widespread multiple intra-abdominal abscesses (Figure 1). Percutaneous drainages were performed, and elevated amylase levels in drained fluids indicated that these abscesses originated from infected pancreatic cysts. *Staphylococcus* species was isolated from a culture of the drained fluid. Despite several recurrences during the next 3 months, remissions of intra-abdominal abscesses were obtained thereafter. At present, 24 months after pancreatitis, she is still undergoing total parenteral nutrition and haemodialysis.

Our patient had no common cause for pancreatitis, such as gallstone, alcohol, metabolic aetiologies, drugs or trauma. Previous reports, however, indicate that either chronic malnutrition, or refeeding after periods of malnutrition, may contribute to the occurrence of pancreatitis [1,2]. Previous reports have also shown that dialysis patients, especially patients receiving long-term peritoneal dialysis, have an increased risk for acute pancreatitis [4]. Nevertheless, malnutrition has not been recognized as an aetiological factor for pancreatitis in CAPD patients. Recently, a case of acute pancreatitis associated with malnutrition due to depressive disorder, as was observed in our case, was reported [2]. Depression is the most common psychological problem in dialysis patients, commonly associated with poor oral intake and aggravated malnutrition [5]. Thus, we should bear in mind that, in CAPD patients, pancreatitis may develop in association with malnutrition, possibly due to depressive disorder, and may cause serious complications such as pancreatic abscesses.

Conflict of interest statement. None declared.

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