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Pharmacokinetic analysis of docetaxel during haemodialysis in a patient with locally advanced non-small cell lung cancer

Sir,

Management of localized stage III non-small cell lung cancer (NSCLC) patients has improved significantly in recent years. Nevertheless, there exist few case reports about chemotherapeutic regimens of patients with end-stage renal disease (ESRD) and NSCLC [1,2]. Docetaxel (DXL) in combination with carboplatin is successfully used in the treatment of NSCLC [3], but there are no reports on the treatment of haemodialysis (HD) patients with NSCLC.

Here, we report on a patient with a NSCLC, who developed ESRD after two cycles of chemotherapy with a gemcitabine/platinum combination. Because of the good performance status of the patient and the chemo-sensitivity of the tumour, treatment was completed with DXL 65 mg/m² and carboplatin 200 mg/m² on day 1 and day 21 with sequential radiotherapy. DXL was infused over 1 h, followed by carboplatin infusion over 1 h. HD was immediately performed after the end of carboplatin application. Total plasma concentrations of DXL were evaluated in the blood samples collected 1, 3 and 5 h after the end of the DXL infusion, using solid phase extraction and high-performance liquid chromatography. Pharmacokinetic analysis of DXL revealed a rapid decrease of plasma concentrations immediately after administration. Only very low amounts of DXL—comparable with plasma concentrations of patients without renal failure—were detected 1 h after the end of the infusion of 65 mg/m² DXL (Figure 1), suggesting that DXL is rapidly bound to plasma proteins as described before [4]. DXL was not dialysed, since increased concentrations were found in plasma samples collected from the venous line compared with samples collected from the arterial line (Figure 1A). Interestingly, even lower amounts of DXL in the blood were found after the second cycle of

Fig. 1. Renal imaging and mutation analysis. (A) renal CT-scan showing calcifications in the renal parenchyma (white arrows). (B) the BSND c.139G>A transition, resulting in Gly to Arg substitution at position 47, is indicated by *. The nucleotides are numbered after the cDNA sequence of BSND (wt, wild type).
DXL (Figure 1B). This observation could be explained by the rapid half-life of DXL (about 4 min) causing no accumulation of the drug in the central compartment after repeated administration. So these differences in DXL plasma concentrations looked accidental. The observed transient increase of DXL plasma concentrations during HD is probably due to altered protein binding of the drug. To evaluate DXL toxicity, blood-count controls were taken in periodic intervals. Grade 2 leuco- and thrombocytopenia (National Cancer Institute Common Toxicity Criteria, NCI-CTC) were detected 10-20 days after the second cycle of chemotherapy (data not shown).

Restaging at day 42 revealed further regression of the central tumour and a decreased bronchial wall thickness. The mediastinal lymph nodes remained stable and a restaging mediastinoscopy showed necrosis but also residual tumour cells. Afterwards, sequential radiotherapy of the mediastinum and the primary completed the treatment.

In conclusion, a carboplatin/DXL combination might be a suitable regimen for NSCLC patients undergoing HD.

Conflict of interest statement. None declared.

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Fig. 1. Pharmacokinetic analysis of DXL. Plasma samples taken before and after the HD capillary were taken 1, 3 and 5 h after the end of DXL infusion. Samples were analysed by HPLC for the total plasma concentration of DXL. (A) DXL plasma levels in samples taken from the arterial (white) and venous line (black). (B) DXL plasma levels taken from the venous line during HD after the first (black) and second cycle of chemotherapy (white).

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Decreased serum fetuin-A levels after a single haemodialysis session

Sir,
Cardiovascular disease (CVD) is the leading cause of mortality in haemodialysis (HD) [1]. Elevated incidence of vascular calcification (VC) is observed in HD. Fetuin-A (AHSG, α2-Heremans–Schimd glycoprotein) is an important inhibitor of VC [2]. Reduced serum fetuin-A levels are associated with inflammation and increased CV mortality in HD [3]. In this study, we examined the effects of a single haemodialysis session on serum fetuin-A levels and other markers of inflammation, such as C-reactive protein (CRP), fibrinogen and albumin. We evaluated 20 clinically stable patients (40% males), aged 67 ± 12.8 years, with an HD vintage >9 months, 50% in standard bicarbonate-HD and 50% in haemodiafiltration (HDF). Serum levels of fetuin-A, CRP, fibrinogen and albumin were measured at the beginning and at the end of a 4-h HD session. Table 1 shows that serum CRP, fibrinogen and albumin levels did not change during the HD session. In contrast, serum fetuin-A levels decreased significantly after 4 h of HD (P = 0.027). We did not observe significant differences in serum fetuin-A levels between patients treated with standard bicarbonate-HD and HDF. The present study confirms that HD patients have reduced serum fetuin-A levels compared with the normal population. Furthermore, serum levels of fetuin-A decreased during a single HD session. Inflammation is one of the most important non-traditional cardiovascular risk factors associated with VC in HD patients. The inflammatory processes induced by HD treatment might contribute to reduced fetuin-A levels and therefore to increased mortality, even if this process does not seem to be improved by convective treatment.

Table 1. Inflammatory markers during a single HD session

<table>
<thead>
<tr>
<th>Marker</th>
<th>Pre-HD</th>
<th>Post-HD</th>
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<tbody>
<tr>
<td>Fetuin-A (g/l)</td>
<td>0.26 ± 0.06</td>
<td>0.21 ± 0.06*</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>9.5 ± 1.3</td>
<td>8.9 ± 1.2</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>3.77 ± 0.48</td>
<td>3.91 ± 0.33</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>351 ± 87</td>
<td>415 ± 93</td>
</tr>
</tbody>
</table>

*P = 0.027.