Indinavir pharmacokinetics in haemodialysis

Sir,
Indinavir is a potent HIV-1 protease inhibitor which is frequently used as part of highly active antiretroviral therapy regimen. Since 10–20% of the dose is recovered in the urine as parent compound, it has been suggested that kidney
function was not the major determinant of the elimination of indinavir. There are only two observations on the pharmacokinetics of indinavir in patients with end-stage renal disease (ESRD) [1,2].

We report here on the pharmacokinetics of indinavir between haemodialysis sessions and during the procedure in an anuric HIV-infected haemodialysis patient with ESRD.

Our patient had no evidence of hepatitis viruses; circulating markers were negative and liver function tests were normal. In November 1995, he began a treatment with zalcitabine, lamivudine and stavudine which was changed in October 1998 to Indinavir 800 mg every 8 h, zidovudine 300 mg/day and lamivudine 300 mg/day. His viral load decreased from 17 500 copies/ml to undetectable levels (<200 copies/ml).

Studies of the pharmacokinetics of indinavir in plasma, conducted between haemodialysis sessions, were performed 6 months after the start of indinavir treatment. Paired arterial and venous blood samples were also performed simultaneously 2 h after the start of a haemodialysis session. Plasma concentrations were determined by high-performance liquid chromatography. Indinavir was administered at the start of the session. Haemodialysis was performed for 4 h using a F60 polysulphone dialysy (surface area 1.4 m²) at a constant dialysate flow of 500 ml/min. Blood flow was held constant at 250 ml/min. The pharmacokinetic parameters of Indinavir in our patient and reference values in HIV-infected patients with normal renal function are summarized in Table 1. No difference was observed in area under the concentration-time curve (AUC) and elimination half-life (T1/2) of Indinavir between reported values and those of our patient. Therefore, dosage modification of Indinavir in HIV-infected patients with ESRD and normal liver function did not seem to be necessary.

In our patient, haemodialysis clearance of indinavir was very low (3.25 ml/min), close to the report of Fiedler et al. [1] (3 ml/min), and another unpublished personal observation (10 ml/min) but differed from the value reported by Guardiola et al. [2] (185 ± 7.2 ml/min). Since indinavir has a large protein-bound fraction (60%) and short half-life, our results were, however, not unexpected and were similar to those reported by Fiedler et al. [1]. Therefore, haemodialysis may be done independently of Indinavir dosing interval.

During the first 6 months of treatment, no clinical or biological side-effects were observed. In particular nephrolithiasis, haemolytic anaemia, insomnia, hypertriglyceridaemia, hyperbilirubinaemia or diabetes did not develop; platelet and leucocyte counts and liver enzymes remained stable. Furthermore, we observed a substantial decrease in viral load. We thus confirm that Indinavir may be adminis-