Cefepime-related neurotoxicity in a haemodialysis patient

Sir,

Our patient was a 40-year-old anuric end-stage renal failure patient on long-term haemodialysis (HD) since 1997. In May 1998, he suffered from an attack of bronchopneumonia with septicaemia. In view of his critical condition, intravenous cefepime at a dose of 1 g every 12 h was started empirically for him. Five days after the commencement of the antibiotic therapy (cumulative dose of 12 g cefepime with one haemodialysis session offered 4 days after cefepime therapy), he became disoriented with waxing and waning mental state followed by an attack of generalized tonic-clonic convulsion. Physical examination showed that he had flapping tremor and generalized myoclonic jerks. His body weight and height were 55 kg and 163 cm, respectively. Computed tomography of the brain was normal. A presumptive diagnosis of cefepime-induced seizure was made. Dose of cefepime was reduced to 1 g every 24 h and was stopped on the next day. Urgent haemodialysis was arranged for him daily for a consecutive of 3 days and then he resumed his previous HD schedule (two times per week). After the first 4 h of urgent haemodialysis, there was a drastic improvement in his conscious level. He had a complete recovery from his mental confusion after the second haemodialysis session. His clinical course was subsequently stable and he was discharged 1 week later. A retrospective analysis of the serum cefepime levels (the first

cefepime level being measured around 9 h after the last dose of cefepime) was made by means of a reverse-phase high performance liquid chromatography technique. The pre-HD–post-HD cefepime levels after the first, second and third urgent HD session were 105–15 μg/ml, 66–10 μg/ml, 9.7 μg/ml–(not available), respectively.

Comment. Cephalosporins have been cited as a cause of drug-induced seizure [1]. The proconvulsant potency is likely related to the competitive antagonistic action at the gamma-aminobutyric acid complex which is the principal inhibitory neurotransmitter in the brain [1]. Cefepime is a fourth-generation cephalosporin with activity against both Gram-positive and Gram-negative organisms. It is widely used for the empirical treatment of serious infections. The elimination half-life of cefepime was approximately 2 h with peak serum concentrations of around 80 μg/ml for 1-g dose and 160 μg/ml for 2-g dose in patients with normal renal function. Total body clearance was around 120–150 ml/min with a volume of distribution of 18 litres [2]. There is a significant effect of renal impairment on the elimination half-life and clearance of cefepime. The plasma binding is only 15%, and half-life of cefepime is prolonged to more than 13 h in patients with end-stage renal failure [3]. Cefepime is dialysable and up to 70% of a given dose may be removed during a 3-h HD session [2]. A dose of 1 g every 24 h is generally recommended for septic patients with GFR < 10 ml/min [2]. A supplemental dose of cefepime is recommended at the end of a HD session. In patients on continuous ambulatory peritoneal dialysis, the elimination half-life of cefepime is about 18 h and a parenteral dose of 1000–2000 mg every 48 h has been shown to be safe and effective for the treatment of systemic infection [4]. Continuous venovenous haemodiafiltration (CVVHD) is another effective way for cefepime elimination. In patients on CVVHD, no dosage adjustment is necessary and the usual dosage regime for patients with normal renal function should be employed [5].

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1. Wallace KL. Antibiotic-induced convulsions. *Crit Care Clin* 1997; 13: 741–762
2. Rybak M. The pharmacokinetic profile of a new generation of parenteral cephalosporin. *Am J Med* 1996; 100 [Suppl 6A]: 39–44
3. Barbhaiya RH, Knupp CA, Forgue ST, Matzke GR, Guay DR, Pittman KA. Pharmacokinetics of cefepime in subjects with renal insufficiency. *Clin Pharmacol Ther* 1990; 48: 268–276
4. Barbhaiya RH, Knupp CA, Pfeffer M, Zaccardelli D, Dukes GM, Mattern W, Pittman KA, Hak LJ. Pharmacokinetics of cefepime in patients undergoing continuous ambulatory peritoneal dialysis. *Antimicrob Agents Chemother* 1992; 36: 2576
5. Allaouchiche B, Breilh D, Jaumain H, Gaillard B, Renard S, Saux MC. Pharmacokinetics of cefepime during continuous venovenous hemodiafiltration. *Antimicrob Agents Chemother* 1997; 41: 2424–2427