Cefazolin-Induced Encephalopathy in a Uraemic Patient

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Dear Sir,

In a recent paper, J.D. Schwankhaus et al. [2] reported the occurrence of an encephalopathy in a uraemic patient who had received a high dose of cefazolin: A 62-year-old man received 2 g cefazolin intravenously every 6 h to treat gram-negative septicemia. Blood creatinine was 10.4 mg/dl. Twenty-four hours later he had a generalized tonic-clonic seizure followed by lethargy, disorientation, asterixis and multifocal myoclonus. Cefazolin dosage was reduced, and within 48 h his mental status improved and neurological signs disappeared.

We would like to report a similar observation in a haemodialysed 41-year-old female whose renal failure resulted from focal and segmental hyalinosis. Haemodialysis treatment was initiated in 1973, and the patient received a renal transplant in 1975. In 1982, osteonecrosis of the femoral head required a hip prosthesis. In 1983, because of recurrence of hyalinosis in the transplant, the patient returned to haemodialysis, during 4 h three times a week. A few days before reinitiation of haemodialysis two clonic seizures occurred and were attributed to metabolic disorders. However, 5 mg phenobarbital per day was prescribed. In January 1984, an abscess around the hip prosthesis was found to be due to *Staphylococcus aureus*. The patient received 50 mg tobramycin in a 1-hour perfusion after each dialysis (3 times per week) and 3 g cefazolin intravenously per day. Eleven days after the outset of the treatment – the patient had received 33 g cefazolin –, a clonic seizure was observed during the dialysis. The barbituric blood level was considered to be insufficient (16 $\mu\text{mol/l}$) and the daily dose of phenobarbital was increased to 15 mg/day. Antibiotic treatment was continued at the same doses. One week later a status convulsivus occurred, which resisted 3 injections of diazepam. Respiratory distress required intubation and assisted breathing. Cerebral tomodensitometric results were normal. Drug toxicity was suspected: 48 h after stopping cefazolin, drug plasmatic concentration was still 280 $\mu\text{g/ml}$, i.e., ten times the effective treatment level.

Dialysis was performed daily, and dialysate concentrations of cefazolin were 100–116 $\mu\text{g/ml}$. The frequency of convulsive episodes decreased, but they ended only 4 days after stopping cefazolin treatment. 75 mg Dibekacin after each dialysis and 1 g erythromycin per day were then prescribed for 9 days. On the 10th day, cefazolin was reintroduced at a dose of 500 mg after each dialysis. Blood levels of cefazolin were determined before each dialysis and did not exceed 128 $\mu\text{g/ml}$.

Pharmacokinetics of cefazolin [1] in healthy volunteers has shown that the plasma half-life of the drug is $1.33 \text{ h} \pm 33 \text{ min}$, but in dialysis patients the half-life increased to $32.42 \text{ h} \pm 9.18 \text{ h}$. Therefore, an accumulation of cefazolin may induce neurologic complications in uraemic patients. In case of severe renal failure it is absolutely necessary to modify the usual prescription, and we suggest, for haemodialysis patients, an intravenous dose of 500 mg cefazolin at the end each haemodialysis.

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