

Cefepime-induced encephalopathy in patient without renal failure

Encefalopatia induzida por cefepime em paciente sem insuficiência renal

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ABSTRACT

This case report describes neurotoxicity in an older patient on cefepime 2 g twice a day. The 81-year-old male patient developed non-convulsive status epilepticus during cefepime treatment with 1 g twice a day. There was recovery 30 days after discontinuation of cefepime.

Keywords: Cephalosporins/adverse effects; Cephalosporins/toxicity; Status epilepticus/Chemically induced; Aged; Case reports

RESUMO

Este relato descreve neurotoxicidade em um paciente mais idoso em uso de cefepime na dose de 2 g duas vezes ao dia. O paciente de 81 anos desenvolveu estado epiléptico não-convulsivo durante o tratamento com 1 g de cefepime duas vezes ao dia. O paciente se recuperou depois de 30 dias, após a interrupção do cefepime.

Descritores: Cefalosporinas/efeitos adversos; Cefalosporinas/toxicidade; Estado epiléptico/induzido quimicamente; Idoso; Relatos de casos

INTRODUCTION

The existence of acute confusional states associated with the use of cephalosporins in patients with variable degrees of renal failure has been well described. Cephalosporins, particularly cefepime, have been associated with status epilepticus (SE)⁽¹⁻⁴⁾. Previous reports focused only patients with no dose adjustment in renal failure. There are several reports of neurotoxicity due to cephalosporins⁽¹⁻⁵⁾, but these involve mostly adults

with acute or chronic renal failure or those on dialysis, although there are similar case reports for children as well^(6,7). There is a significant effect of renal impairment of the elimination half-life and clearance of cefepime. A dose of 1 g every 24 hours is recommended for patients with glomerular filtration rate (GFR) lower than 10 mL/min⁽⁸⁾. In a study with young male mice (maximum age between six and eight weeks), doses up to 1000 mg/kg (i.v.), did not induce convulsions in normal conscious mice and rats; however, it produced convulsions in experimental animals with extensive renal failure⁽⁹⁾. In elderly patients, renal function decreases and it is important to adjust the cefepime dose when creatinine clearance is lower than 50 mL/min⁽¹⁰⁾.

CASE REPORT

An 81-year-old Caucasian diabetic man was admitted for spinal surgery and developed pneumonia. Cefepime 2 g/day was added to his antibiotic regimen to broaden *Pseudomonas aeruginosa* coverage. The patient started on intravenous ceftriaxone and clarithromycin for ten days before being given cefepime at 1 g twice a day instead. After six days of cefepime, he became confused. The neurological examination showed no focal deficits. Computed tomography (CT) of the brain was normal. Cerebrospinal fluid (CSF) examination was negative, and liver function was normal. His renal function deteriorated over 24 hours, 5 days before he displayed neurological symptoms (Table 1). Two days after the onset of mental status changes, an electroencephalography

Study carried out at Internal Medicine (Neurology) of Hospital Israelita Albert Einstein – HIAE, São Paulo (SP), Brazil.

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Received on Nov 26, 2009 – Accepted on Apr 22, 2010

(EEG) revealed diffuse slow-wave activity (delta) and triphasic sharp-wave activity (Figure 1). Cefepime was discontinued, and four days later he was less confused and the new EEG (Figure 2) revealed only diffuse delta. Within 30 days after discontinuation of cefepime, the patient showed recovery in mental status and was able to respond appropriately to questions.

Table 1. Creatinine evolution during cefepime treatment

Day	-10	-7	-5	-4	-3	1	3	4	5	6	7	9	11	17
Creatinine (mg/dl)	1.1	1.1	1.3	1.4	1.2	1.0	1.9	1.3	1.1	1.0	1.0	1.1	1.0	1.0
Blood urea nitrogen (mg)	15	11	17	34	37	20	44	48	39	39	39	47	39	21

Cefepime was started in the day 1 and symptoms began in the day 10.



Figure 1. First electroencephalogram showing generalized sharp and slow wave discharges

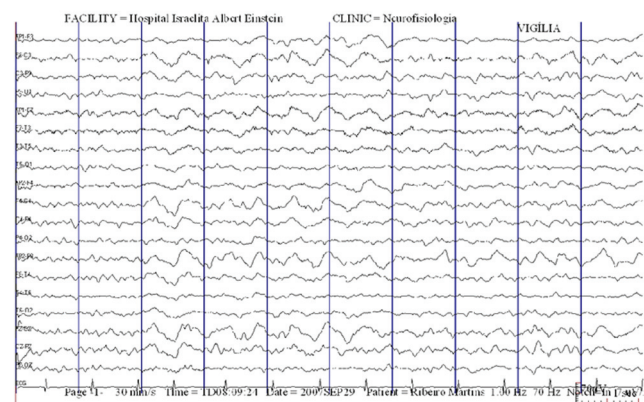


Figure 2. Second electroencephalogram showing generalized delta activities, after cefepime was discontinued

DISCUSSION

Beta-lactam antibiotics produce convulsions via their gamma-aminobutyric acid (GABA) antagonist properties and by enhancing glutamate-mediated excitatory neurotransmission⁽⁹⁾. Convulsive activities of different β -lactam antibiotics were investigated using intracerebroventricular (ICV) administration in mice. Cefepime has relatively potent intrinsic convulsive activity⁽¹¹⁾. Some studies demonstrated that

these antibiotics competitively inhibit GABA-induced chloride currents by binding directly to the receptor, thus resulting in an inhibition of an inhibitory response leading to depolarization of the postsynaptic membrane potential⁽¹²⁻¹⁴⁾.

Elderly patients present with decreased creatinine clearance with age. For example, a 70-year-old, 70 kg patient with 1 mg/dl creatinine has a clearance of 45 ml/min. The glomerular filtration rate (GFR) must decline to about half of the normal level before the serum creatinine concentration rises above the upper limit of normal. Monitoring of renal function is needed in older patients with severe disease, sepsis, and those who are receiving nephrotoxic therapy. Specifically in our patient, a serum creatinine of 1.2 mg/dl corresponds to a clearance of 50 ml/min (Figure 3), and requires a dose adjustment of the antibiotic. In elderly patients and normal subjects in medical or surgical wards, the renal function should be checked to allow daily adjustments of the cefepime dose.

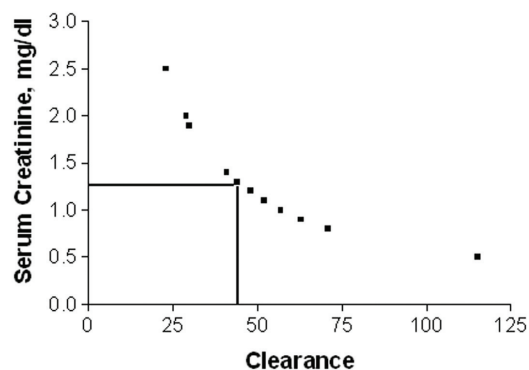


Figure 3. Relationship between creatinine and clearance (by Cockcroft-Gault formula)

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