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Seizures after Imipenam

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Abstract

Imipenam causing epileptic episode is an uncommon finding. It is seen in patient with renal dysfunction and high dose. We present such case in presence of normal renal function and normal clinical dose.

Introduction

Carbapenems are ß-lactam antibiotics with broad-spectrum activity against a variety of infections. Even though the carbapenems have safer clinical profiles, it can cause convulsions by inhibiting gamma amino butyric acid receptor. Neurotoxicity of carbapenem antibiotics is related with the presence of amino group in the C-2 side chain. However, the detail mechanism may be different not only among carbapenems, cephalosporins, and penicillins but among carbapenem compounds themselves. It is important to know the neurotoxic potential of a compound by investigating the effect of direct administration into the central nervous system such as intraventricular administration, since the neurotoxicity of the compound depends on penetration of the drug through blood-brain barrier and its pharmacokinetic properties in critically ill patients. Imipenam can be epileptogenic if dose exceeds excess of 2 g/day and in presence of kidney dysfunction.

Case Report

40 years female patient (weight 58 kg, height 152 cm) with dilated cardiomyopathy was referred to our center in an intubated condition. Chest x ray revealed consolidation in left middle lung zone. Endotracheal secretions were sent for microbiological culture and sensitivity which showed klebsiella pneumoniae growth sensitive to Imipenam antibiotics. Patient was started with intravenous injection Imipenam 500 mg thrice a day. Patient's renal function test and liver function tests were normal. After 5 days of therapy, patient developed generalized tonic clonic convulsions which were managed by injection midazolam. Magnetic resonance imaging (MRI) of brain did not reveal any abnormality. There was no past history of seizures. Patient's medications were reviewed and Imipenam was assumed to be responsible drug. It was substituted by other sensitive drug colistin. Patient did not have any seizure episode thereafter.

Incidences of seizures in critically ill patients was reported to be 0.2 - 3%[1]. Mechanism of Epileptic effect of carbapenems is by inhibiting gamma amino-butyric acid (GABA) mediated inhibitory transmission[2,3]. Elderly age group, brain disease, renal disorder, overdose of carbapenam and use of neurotoxin drugs are the predisposing factors for carbapenam induced neurotoxicity[1]. Renal dysfunction leads to accumulation of carbapenam due to impaired excretion. As the Imipenam is transported to brain tissue by passive diffusion, increased concentration of the drug in renal failure patient is epileptogenic

and neurotoxicity[1]. Convulsion risk can be reduced by adjusting the dose according to renal function. Imipenem when used with cilastatin can be more proconvulsive as Imipenam levels are raised in presence of cilastatin. Cilastatin prohibits its renal tubular secretion and inhibit cerebrospinal fluid elimination. In fact cilastatin when used in higher clinical dose can itself promote convulsions[4].

Sepsis induced inflammatory mediators release in brain causes blood brain barrier dysfunction[5]. In the present case, alteration in blood brain barrier may have resulted more diffusion of drug into brain tissue and causing neurological dysfunction despite normal renal function with no overdosing.

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