DRUG INTERACTION BETWEEN IMIPENEM AND VALPROIC IN BIPOLAR DISORDER: A CASE STUDY

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Background

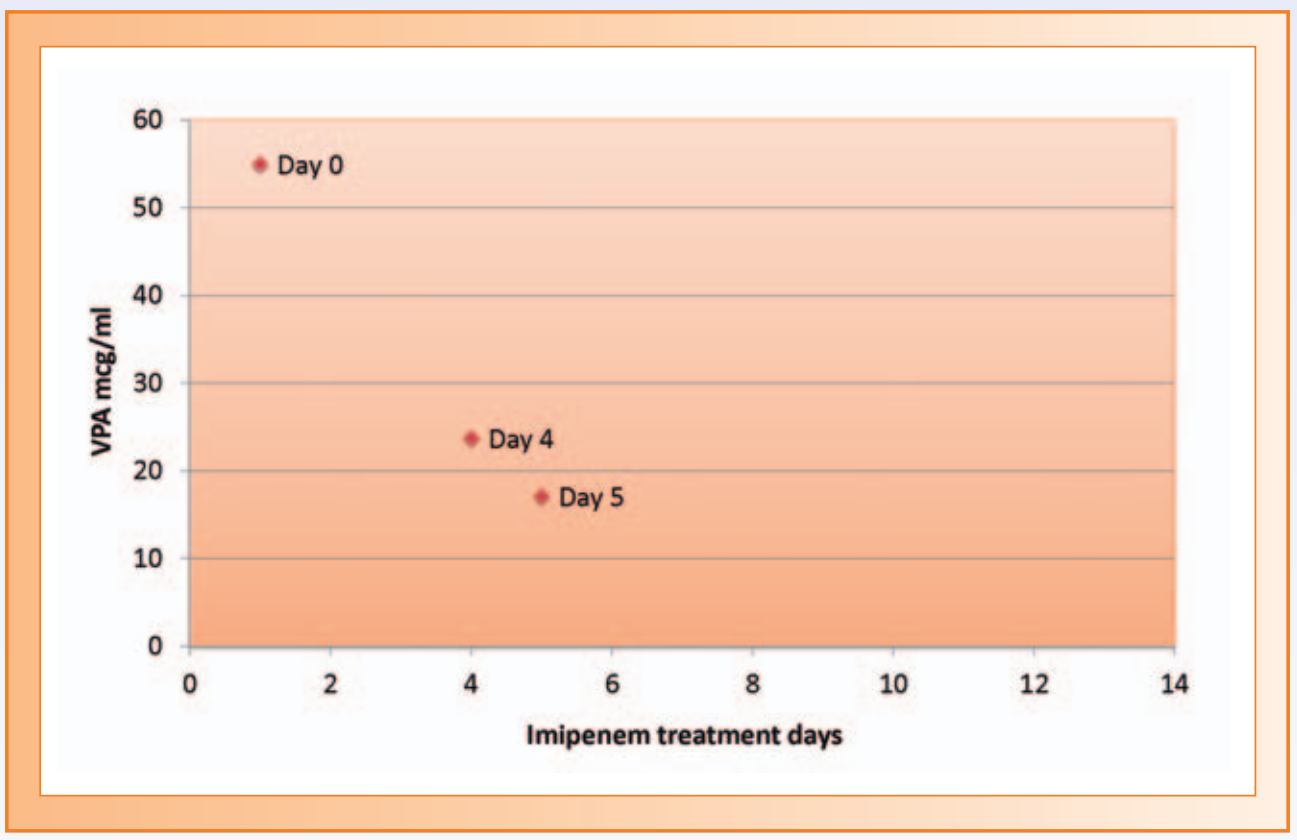
Valproic acid (VPA) is an antiepileptic drug used for the treatment of bipolar disorder (BD). Researchers have studied the effect of valproic interactions through its inhibition of cytochrome P450, though its own pharmacokinetics can be disturbed as well. One specific interaction occurs with carbapenem antibiotics.

Methods

We report the case of a patient with BD, psychologically stable for years, suffering from maniac episode due to carbapenem treatment.

Findings

We are called for a psychiatry assessment of an impatient 80-year-old woman in Infectious Disease Service with a history of BD. The patient has been stable for 30 years with litihum. Two months ago, during an acute respiratory failure, the patient was treated with furosemide. The lithium serum levels increased, as a result of an interaction with the diuretic treatment, leading to acute confusional state. In order to prevent new episodes the lithium was stopped. Currently the patient is under valproic treatment (1000mg per day) as a mood stabiliser. The patient consulted the emergency room for fever receiving empirical treatment with ceftriaxone and ciprofloxacin. Blood cultures were positive for ESBL-E coli and antibiotic treatment was switched to imipenem. Four days after the onset of imipenem the patient showed hyperthymia, irritability, verbiage and sleeping hours reduction. The addition of olanzapina to the habitual treatment was needed to control the symptoms. VPA levels were 23.75mcg/ml (optimal rage is from 50 to 100mcg/ml) descending to 17.13mcg/ml in less than 24 hours. On discharge, imipenem was discontinued and olanzapina maintained. Unfortunately, the patient was lost before a follow-up VPA level was drawn.



Valproic concentration during imipenem treatment

Discussion

The present findings support studies revealing a significant and rapid decrease (70% in less than 24 hours) in VPA levels following initiation of carbapenem therapy. Increasingly VPA daily dose did not return serum concentrations to therapeutic levels while under carbapenem treatment or until a mean of 8 days following discontinuation. More research is needed to understand the mechanism of the interaction. Authors suggest that carbapenems inhibit hydrolysis of VPA-G back to VPA, increasing clearance of VPA. Others propose inhibition of VPA blood distribution and blockage of intestinal absorption. Clinicians should be aware of the possible clinical consequences of this interaction although carbapenems might be of value in the management of VPA overdose.

I do not have conflict of interest