



Valproic Acid and Carbapenems: What's Causing VPA to be MIA?

Valproic acid (VPA) is a common antiepileptic. Carbapenems given with VPA significantly decreases levels of VPA.¹ How much does it decrease? Should providers completely avoid the co-administration of VPA and carbapenems?

Mechanism of carbapenem and VPA drug interaction:

The mechanism is not fully known, but likely occurs through multiple mechanisms. The main proposed mechanism is carbapenem inhibition of a key hydrolytic liver enzyme leading to decreased conversion to active serum VPA.³

Is this drug interaction seen with all carbapenems?

Yes, the interaction has been demonstrated with meropenem, ertapenem, imipenem, and doripenem.³

What happens to VPA levels when given with a carbapenem?

Carbapenems can lead to 60% – 80% reductions in VPA levels.² VPA levels will rapidly decrease within the first 24 hours of administration of a carbapenem and can take 7 - 14 days to return to therapeutic concentrations after carbapenem discontinuation.^{2,3}

How should the drug interaction be managed?

If possible, alternative antimicrobials and/or anti-epileptic drugs (AED) should be used.¹ In patients who must receive a carbapenem, an additional AED should be added during the carbapenem course and be continued until VPA levels return to therapeutic concentrations after carbapenem discontinuation. Patients at low risk for seizures who are expected to receive a short course of therapy may be closely monitored without an additional AED.³

Can't we just increase the VPA dose while using a concomitant carbapenem?

No, reports have demonstrated that VPA serum concentrations can be decreased **irrespective** of total daily dose of VPA. Case reports have demonstrated that patients can experience seizures despite increased doses of VPA.^{3,4}

Key Takeaway: Carbapenems will significantly and rapidly decrease valproic acid levels, putting patients at risk for seizures. The interaction CANNOT be overcome by increasing the valproic acid dose. Carbapenem therapy should be avoided whenever possible. Additional anti-epileptics may be needed while on concomitant carbapenem therapy.

References:

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