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## Letter to the Editor

# Meropenem-induced low valproate levels in a cerebral palsy child



Dear Editor,

Valproate (VPA) is commonly prescribed as first-line agent to control seizure disorders.<sup>1</sup> Concomitant use of cytochrome P450 (CYP) inducers or inhibitors can result in altered VPA absorption or elimination rates. While CYP-based drug interactions are well described, non-CYP interactions are increasingly becoming visible in literature. The importance of non-CYP interaction is exemplified by a case of meropenem-induced VPA serum level reduction in a child with poor neurological prognosis.

A 3-year old boy was admitted to the hospital to investigate a genetic disorder and progressive uncontrolled convulsions. Since 11-months old, when the child was diagnosed with hypotonic cerebral palsy (CP), recurrent episodes of hospitalizations due to bronchiolitis and bronchopneumonia have occurred. On day 1, meropenem and vancomycin were started due to ventilator-associated pneumonia and VPA was progressively escalated from 40 to 70 mg/kg/day, due to uncontrolled convulsions and low VPA serum levels (<2.8 mcg/mL) on day 3. Concomitant drugs included phenobarbital, topiramate and clobazam. When meropenem was switched to piperacillin-tazobactam, VPA levels started to increase (10 mcg/mL) and, two weeks later, achieved 18.6 mcg/mL. The drug interaction was classified<sup>2</sup> as probable (score 6), according to Drug Interaction Probability scale due to well documented evidence on adults<sup>3</sup> and a single study in children.<sup>4</sup> Carbapenems can irreversibly inhibit acylpeptide hydrolase, an enzyme that deconjugates valproate-glucuronide complex and reduces urinary elimination of VPA.<sup>5</sup> The abrupt onset<sup>3-5</sup> (<24 h), the slow<sup>3-5</sup> (7–20 days) time to return to therapeutic levels, and the risks associated with uncontrolled convulsions suggest to consider, when feasible, non-carbapenemic antibiotics in CP children on VPA.

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Lucas Miyake Okumura<sup>a,\*</sup>, Cinara Andreolio<sup>b</sup>,  
Carla Di Giorgio<sup>b</sup>, Paulo Roberto Antonacci Carvalho<sup>b</sup>,  
Jefferson Pedro Piva<sup>b</sup>

<sup>a</sup> Hospital de Clínicas de Porto Alegre, Divisão de Farmácia Clínica, Porto Alegre, RS, Brazil

<sup>b</sup> Hospital de Clínicas de Porto Alegre, Unidade de Terapia Intensiva Pediátrica, Porto Alegre, RS, Brazil

\* Corresponding author.

E-mail addresses: [lucasokumura@yahoo.com.br](mailto:lucasokumura@yahoo.com.br),  
[okumura.lucas@gmail.com](mailto:okumura.lucas@gmail.com) (L.M. Okumura).

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## Conflicts of interest

The authors declare no conflicts of interest.