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The absorption of gabapentin following high dose escalation.

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Abstract

Gabapentins (GBP) is structurally similar to GABA yet its mode of action remains uncertain. It is water-soluble and GI tract absorption occurs via the L-amino acid transport system in the proximal small bowel. It has been suggested that this transportation is capacity limited, thus decreasing GBP bioavailability at higher doses. GBP is not protein bound, therefore, salivary levels might be expected to be similar to those in serum; also the drug does not induce hepatic enzymes and is excreted unmetabolised by the kidney. Within the dose-range normally prescribed, it is devoid of pharmacokinetic (PK) drug interactions with all other anti-epileptic drugs. This study assesses two things in patients with epilepsy: (a) bioavailability of higher doses of GBP (1200-4800 mg per day), and (b) the influence of high dose GBP on between-dose serum concentrations of co-prescribed anti-epileptic drugs. After stabilising at each dosage, a sequence of serum and saliva samples were collected within the dosage interval; GBP and co-medication concentrations were determined and the results subjected to PK modelling. Meaned results from 10 patients indicate that GBP continues to be absorbed in a reasonably linear manner relative to dose up to 4800 mg per day. The study also shows that GBP is transported into saliva, however, salivary concentrations are only 5-10% of those in plasma. Furthermore, the results indicate that GBP, in higher than recommended doses, did not change plasma concentrations of lamotrigine, carbamazepine, carbamazepine-epoxide, vigabatrin, primidone, phenobarbitone or phenytoin when added to treatment. It is concluded that larger than recommended doses of GBP can be efficiently absorbed by some patients and also that GBP plasma levels do not fluctuate greatly between dosage intervals, therefore, twice daily dosage is a possibility.

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