Short communication

Gabapentin synergistically interacts with topiramate in the mouse maximal electroshock seizure model: an isobolographic analysis

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Abstract:
The anticonvulsant effects produced by topiramate (TPM) and gabapentin (GBP) – two second-generation antiepileptic drugs, in numerous fixed-ratio combinations of 8:1, 4:1, 2:1, 1:1, 1:2, 1:4 and 1:8 were examined by isobolographic analysis in the mouse maximal electroshock seizure (MES) model. Results indicate that the combinations of TPM and GBP at the fixed-ratios of 2:1, 1:1, 1:2, 1:4 and 1:8 resulted in supra-additive (synergistic) interaction against MES-induced seizures. Moreover, the combinations of TPM and GBP (at their median effective doses) did not affect motor performance of animals challenged with the chimney test and had no impact on neuromuscular tone in the grip-strength test. Additionally, GBP had no impact on total brain TPM concentrations, and simultaneously, TPM did not alter brain GBP concentrations, indicating that the interaction between drugs was pharmacodynamic in nature. In conclusion, supra-additive interaction of TPM with GBP against MES-induced seizures, lack of motor coordination and neuromuscular tone impairments as well as lack of pharmacokinetic interactions between TPM and GBP in preclinical study, strongly support the combined application of both antiepileptic drugs in patients with refractory partial epilepsy.

Key words:
topiramate, gabapentin, maximal electroshock, isobolographic analysis, pharmacodynamic interaction

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