



Synergistic interaction of gabapentin with tiagabine in the hot-plate test in mice: an isobolographic analysis

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Abstract:

This study was aimed at determining the analgesic effect of gabapentin and tiagabine, two antiepileptic drugs that were administered alone and in combination at a fixed ratio of 1:1, in the acute thermal pain model (hot-plate test) in mice.

Linear regression analysis was used to evaluate the dose-response relationships between logarithms of antiepileptic drug doses and their resultant maximum possible antinociceptive effects in the mouse hot-plate test. From linear equations, we calculated doses that increased the antinociceptive effect by 50% (ED₅₀ values) for gabapentin, tiagabine and their combination. The type of interaction between gabapentin and tiagabine was assessed using the isobolographic analysis.

Results indicated that both antiepileptic drugs produced the definite antinociceptive effect, and the experimentally derived ED₅₀ values for gabapentin and tiagabine, when applied alone, were 504.4 mg/kg and 5.67 mg/kg, respectively. With isobolography, the experimentally derived ED_{50 mix} value for the fixed ratio combination of 1:1 was 139.31 mg/kg and significantly differed from the theoretically calculated ED_{50 add} value, which was 255.04 mg/kg ($p < 0.05$), indicating the synergistic interaction between gabapentin and tiagabine in the hot-plate test in mice.

In conclusion, the combination of tiagabine with gabapentin at a fixed ratio of 1:1 exerted a synergistic interaction in the mouse model of nociceptive pain. If the results from this study could be extrapolated to clinical settings, the combination of tiagabine with gabapentin might be beneficial for pain relief in humans.

Key words:

drug interaction, gabapentin, hot-plate test, isobolographic analysis, maximum possible antinociceptive effect, tiagabine
