Short communication

Effect of N\textsuperscript{G}-nitro-L-arginine on the anticonvulsant action of four second-generation antiepileptic drugs in pentetrazole-induced clonic seizures in mice

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Abstract:
The exact role of compounds modulating nitric oxide (NO) content in the brain during seizure phenomena is under intensive investigation. This study was aimed at determining the effect of N\textsuperscript{G}-nitro-L-arginine (L-NA; a non-selective NO synthase inhibitor) on the anticonvulsant activity of four second-generation antiepileptic drugs (AEDs: gabapentin [GBP], oxcarbazepine [OXC], tiagabine [TGB] and vigabatrin [VGB]) in the mouse pentetrazole (PTZ)-induced seizure model. The acute adverse-effect liability of the studied AEDs in combinations with L-NA were evaluated in the chimney test (motor coordination).

Results indicate that L-NA (40 mg/kg; \textit{ip}) significantly reduced the anticonvulsant activity of OXC in the PTZ test, by increasing its ED\textsubscript{50} from 20.9 to 29.8 mg/kg (p < 0.05). Similarly, L-NA at doses of 20 and 40 mg/kg considerably attenuated the antiseizure effects of VGB by raising its ED\textsubscript{50} from 595 to 930 mg/kg (p < 0.05), and 1022 mg/kg (p < 0.01), respectively. L-NA at lower doses of 10 and 20 mg/kg did not affect significantly the anticonvulsant effects of VGB and OXC in PTZ-induced seizures. Likewise, the co-administration of L-NA (40 mg/kg; \textit{ip}) with GBP and TGB was associated with no significant changes in their anticonvulsant activities in PTZ-induced seizures in mice. Moreover, none of the examined combinations of L-NA (40 mg/kg; \textit{ip}) and second-generation AEDs (at their ED\textsubscript{50} values) affected motor coordination in the chimney test.

Based on this preclinical study, one can conclude that L-NA reduced the anticonvulsant activities of VGB and OXC in the mouse PTZ-induced seizure model. Only, GBP and TGB were resistant to the action of L-NA in this model.

Key words: 
N\textsuperscript{G}-nitro-L-arginine, nitric oxide, oxcarbazepine, vigabatrin, pentetrazole-induced seizures, tiagabine, gabapentin, mice