INFLUENCE OF VIGABATRIN, A NOVEL ANTIEPILEPTIC DRUG, ON THE ANTICONVULSANT ACTIVITY OF CONVENTIONAL ANTIEPILEPTICS IN PENTETRAZOLE-INDUCED SEIZURES IN MICE

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Vigabatrin is a novel antiepileptic drug, which increases GABA levels by irreversible inhibition of GABA-aminotransferase. The aim of this study was to evaluate the effects of vigabatrin on the anticonvulsant activity of valproate, ethosuximide and clonazepam against pentetrazole-induced seizures in mice. In addition, the effects of antiepileptic drugs alone or in combination with vigabatrin were studied on motor performance and long-term memory. Chemical seizures were induced by subcutaneous injection of pentetrazole at its CD₅₀ and defined as a clonus of the whole body with an accompanying loss of righting reflex, lasting for over 3 s. Vigabatrin inhibited the clonic pentetrazole-induced seizures and ED₅₀ of the drug was 879 mg/kg. Vigabatrin (at the subthreshold dose of 250 mg/kg) potentiated the protective activity of ethosuximide, reducing its ED₅₀ from 142 to 95 mg/kg against clonic seizures induced by pentetrazole, but simultaneously elevated its plasma level. The protective activity of valproate and clonazepam remained almost unchanged. However, vigabatrin (250 mg/kg) decreased TD₅₀ (50% toxic dose – corresponding to the impairment of motor coordination in 50% of the animals) of ethosuximide and clonazepam from 549 and 3.84 to 460 and 1.1 mg/kg, respectively, in the chimney test. Vigabatrin (250 mg/kg) did not influence TD₅₀ value of valproate in this test. Vigabatrin (at the dose of 250 mg/kg) did not impair long-term memory in combination with antiepileptics. Potentiation of the ethosuximide’s protective activity was apparently due to a pharmacokinetic interaction. Consequently, no pharmacodynamic interactions between vigabatrin and the studied conventional antiepileptic drugs were evident.

Key words: vigabatrin, antiepileptic drugs, pentetrazole-induced seizures

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