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Digoxin enhances the effect of antiepileptic drugs with different mechanism of action in the pentylenetetrazole-induced seizures in mice

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ABSTRACT

The worldwide prevalence of epilepsy with high percentage of multidrug-resistant patients make it urgent to find new approaches to treating, including the use of combinations of classic anticonvulsants with drugs that have an exclusively original mechanism of action, in particular digoxin. The aim of this work was to investigate the influence of low-dose digoxin on the anticonvulsant effect of sodium valproate, topiramate, levetiracetam, phenobarbital and clonazepam. A basic model of pentylenetetrazole-induced seizures in mice was used. Antiepileptic drugs were administered intragastrically in conditionally effective (ED_{50}) and sub-effective (½ ED_{50}) doses at 30 min, digoxin – subcutaneously at a dose of 0.8 mg/kg ($^1/_{10}$ LD_{50}) at 10–15 min before seizures induction. Pentylenetetrazole at a dose of 80 mg/kg was administered subcutaneously. Experimental data demonstrates that cardiac glycoside digoxin enhances the anticonvulsant activity of sodium valproate, topiramate, levetiracetam, phenobarbital and clonazepam in the model of pentylenetetrazole-induced seizures, providing a clear protective effect of their sub-effective doses. Digoxin may be a valuable component of adjuvant pharmacotherapy for epilepsy, as it reduces the doses of the classic AEDs without compromising the effectiveness of treatment.