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Digoxin potentiates the anticonvulsant effect of antiepileptic drugs against experimental seizures in mice

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Introduction: The great amount of epilepsy patients in the world with a large percentage of multidrug-resistant forms [1] determine the urgency of developing new approaches to treatment. From separate early studies [2, 3], there is evidence of a pronounced anticonvulsant effect of cardiac glycoside digoxin. However, the influence of digoxin on anticonvulsant effect of classical antiepileptic drugs (AEDs) remain unknown. The aim of the study is investigating the influence of low doses of digoxin on the anticonvulsant effect of the most widely used AEDs – carbamazepine, lamotrigine, sodium valproate, topiramate, levetiracetam, phenobarbital and clonazepam.

Materials and methods: The experiments were conducted on male albino mice. Basic models of pentylenetetrazole-induced seizures and maximal electroshock were used [4]. AEDs 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 15 min before seizures induction. Pentylenetetrazole at a dose of 80 mg/kg was administered subcutaneously. The maximal electroshock was reproduced by transmitting an electric current (strength – 50 mA, frequency – 50 Hz) through the corneal electrodes for 0.2 sec.

Results: Co-administration of digoxin with AEDs in sub-effective doses render a marked anticonvulsant activity on the model of pentylenetetrazole-induced seizures. In addition, digoxin potentiates the effects of all AEDs against convulsions induced by maximal electroshock, providing a distinct protective effect of anticonvulsant medicines in sub-effective doses. It should be mentioned that the pronounced anticonvulsant effect of the combinations "digoxin + AED" is detected even if the mechanism of action of the corresponding AED does not match the pathogenesis of the seizure model.

Conclusions: Digoxin can be a perspective component of complex therapy of epilepsy (including multidrug-resistant one) as it reduces the doses of the antiepileptic drugs with a corresponding reduction in the risk of side effects without compromising treatment efficacy.

References

1. Kalilani L, Sun X, Pelgrims B, Noack-Rink M, Villanueva V. The epidemiology of drug-resistant epilepsy: A systematic review and meta-analysis. Epilepsia. 2018;59(12):2179–2193.
2. Markova I, Mikhaĭlov I, Guzeva V. Digoksin – aktivnoe protivoepilepticheskoe sredstvo [Digoxin – an active antiepileptic agent]. Farmakologiia i toksikologiia – Pharmacology and toxicology. 1991;(54)5:52–54. [in Russian]
3. Shtrygol' S, & Shtrygol' D. Digoksin kak protivoepilepticheskoe sredstvo u detei (kliniko-eksperimental'noe issledovanie) [Digoxin as an antiepileptic in children (clinical and experimental study)]. Ukrayinskyi medychnyi al'manakh – Ukrainian Medical Almanac. 2010;13(4):164. [in Russian]
4. Mironov A, Bunyatyan N, Vasileva A (Eds.). Rukovodstvo po provedeniyu doklinicheskih issledovaniy lekarstvennyih sredstv. Ch. 1 [Guidelines for conducting pre-clinical trials of medicines. Part one]. 2012. Moscow: Grif and K. [in Russian]