

confirmation of IDA is reduced transferrin saturation, increased concentration of protoporphyrin erythrocytes, increased concentration of transferrin.

The patient's treatment consists of eliminating the cause of IDA according to the established diagnosis and pharmacotherapy. Pathogenetic pharmacotherapy is usually performed with the help of iron medications for oral administration (preference is given to divalent iron medications). The dose of iron is prescribed in terms of elemental iron. The therapeutic dose of the drug is prescribed individually at the rate of 2 mg/kg of body weight of the patient. The following medications of divalent iron in oral forms are recommended: iron sulfate, iron fumarate. Also preparations of trivalent ferric iron in oral forms: iron oxide saccharate, iron (III) hydroxide complex with polymaltose. Parenteral iron medications are prescribed only for special indications. These are iron carboxymaltose, iron (III) hydroxide-sucrose complex. Also in the pharmacotherapy of IDA is used such iron supplements in combination with folic acid as iron fumarate with folic acid; iron (III) hydroxide complex with polymaltose and folic acid; iron sulfate with folic acid. In addition, there are iron supplements in combination with other drugs: iron fumarate with folic acid and cyanocobalamin; iron ammonium citrate with folic acid and cyanocobalamin; iron fumarate with folic acid, cyanocobalamin, ascorbic acid and zinc sulfate; iron sulfate with ascorbic acid; iron sulfate heptahydrate with ascorbic acid; iron gluconate, manganese gluconate with copper gluconate; iron sulfate heptahydrate with D, L-serine.

Conclusions. The results of the analysis of the collected information indicate that the correct diagnosis is necessary for effective pharmacotherapy of IDA. Treatment of iron deficiency anemia should be carried out according to the clinical protocol using the following list of drugs.

DIGOXIN AT SUB-CARDIOTONIC DOSES INCREASES THE ANTICONVULSIVE POTENTIAL OF CLASSICAL ANTI-EPILEPTIC DRUGS ON THE EXPERIMENTAL SEIZURES INDUCED BY CAMPHOR

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Introduction. The widespread prevalence of epilepsy in the world population, together with the high percentage of patients resistant to existing antiepileptic drugs (AEDs), stimulate the constant search for new approaches to the treatment of the disease. One of the promising ways to improve the treatment of epilepsy is the use of drugs with new targets – the original basic mechanism of action, not inherent in the known AEDs. The anticonvulsant potential of drugs from different pharmacological groups – the so-called "non-antiepileptic drugs" – in particular, antiarrhythmic drugs, nonsteroidal anti-inflammatory drugs, synthetic antidiabetic drugs, statins etc. In addition, there are experimental justifications for potentiation by low doses of cardiac glycoside digoxin of the effect of classical AEDs in sub-effective doses on the basic model of pentylenetetrazole-induced seizures. Clinical data on the efficacy of sub-cardiotonic doses of digoxin as an off-label adjuvant in patients with multidrug-resistant epilepsy were also obtained. However, the optimal combinations of classical anticonvulsants and digoxin in convulsions with various neurochemical mechanisms, including conditions of cerebral monoamine imbalance (for example, on the experimental camphor-induced seizures), remain unknown.

Aim. The aim of the study was to find out the effects of digoxin at a sub-cardiotonic dose on the anticonvulsant effect of seven classical anti-epileptic drugs (AEDs) – sodium valproate,

carbamazepine, lamotrigine, levetiracetam, topiramate, phenobarbital and clonazepam – on a model of seizures induced by camphor in mice.

Materials and methods. The research was implemented within the framework of scientific-research program of the Ministry of Health of Ukraine “Rationale for improving the treatment of multidrug-resistant epilepsy through the combined use of classical anticonvulsant medicines with other drugs” (Order of the Ministry of Health of Ukraine № 509 from 24 February 2020), carried out at the expense of the State Budget of Ukraine. The study was conducted on albino male mice weighing 20-24 g, which were kept on a standard diet with free access to water in controlled vivarium conditions at constant humidity and temperature + 18-20 ° C on the basis of the Central Scientific and Research Laboratory of the Educational and Scientific Institute of Applied Pharmacy of the National University of Pharmacy. Animals were randomly divided into groups: control (untreated seizures), animals with model seizures receiving digoxin, animals with convulsions administered sodium valproate, levetiracetam, topiramate, phenobarbital, clonazepam, and their combinations with digoxin. Classical AEDs were administered once intragastrically at conditionally effective (ED_{50}) and sub-effective ($\frac{1}{2} ED_{50}$) doses 30 min before seizure induction: sodium valproate and topiramate – at doses of 300 and 150 mg/kg; levetiracetam and carbamazepine – at doses of 100 and 50 mg/kg; lamotrigine – at doses of 25 and 12.5 mg/kg; phenobarbital – at doses of 20 and 10 mg/kg; clonazepam – at doses of 0.1 and 0.05 mg/kg. Digoxin was administered once subcutaneously at a dose of 0.8 mg/kg 15 min before seizure induction. Camphor in the form of an oil solution at a dose of 1000 mg/kg was administered to animals intraperitoneally. Statistical analysis of the obtained results was performed using the software package STATISTICA 12 (StatSoft, USA) with the calculation of the mean, standard error of mean, p-value. Significance of differences between comparison groups was evaluated by the non-parametric Mann-Whitney U-test as well as Fisher's angular transformation (for the results in an alternative form).

Results and discussion. According to the influence on the main indicators of the severity of seizures (animals' lethality, the latency period of the first attacks, the number of clonic-tonic seizures per 1 mouse) it was found that digoxin in a sub-cardiotonic dose not only shows quite pronounced anticonvulsant properties in the camphor-induced seizure model, but also potentiates the anticonvulsant effect of some classical AEDs at sub-effective doses. The anticonvulsant effect of the combination of digoxin with sodium valproate at a $\frac{1}{2} ED_{50}$ was not inferior to the anticonvulsive activity of the corresponding AED at an ED_{50} . When digoxin was co-administered with topiramate and phenobarbital, the anticonvulsant effect of the combinations "AED at $\frac{1}{2} ED_{50}$ + digoxin" even exceeded the activity of the corresponding AED at an ED_{50} . The obtained results suggest digoxin to affect the metabolism of cerebral monoamines and justify further in-depth study of the anticonvulsant potential of this cardiac glycoside under experimental seizures with other neurochemical mechanisms (in particular, induced by picrotoxin, thiosemicarbazide, caffeine, pilocarpine, etc.).

Conclusions. Thus, in a model of camphor-induced seizures in mice, digoxin at a sub-cardiotonic dose was shown to significantly potentiate the effects of classical AEDs, especially sodium valproate, topiramate and phenobarbital, providing a clear protective effect of their sub-effective doses. Digoxin allows to reduce doses of classical anticonvulsant medicines and, accordingly, risks of side effect not only without decrease, but also with increase in efficiency of treatment.