Міністерство охорони здоров'я України
Національний фармацевтичний університет
Інститут підвищення кваліфікації спеціалістів фармації
Кафедра клінічної фармакології

АКТУАЛЬНІ ПИТАННЯ КЛІНІЧНОЇ ФАРМАКОЛОГІЇ ТА КЛІНІЧНОЇ ФАРМАЦІЇ (TOPICAL ISSUES OF CLINICAL PHARMACOLOGY AND CLINICAL PHARMACY)

Матеріали науково-практичної
Internet-конференції з міжнародною участю
28 жовтня 2025 року
м. Харків

Харків
НФаУ
2025

EXPERIMENTAL JUSTIFICATION OF THE USE OF "NON-ANTIEPILEPTIC" DRUGS IN COMPLEX PHARMACOTHERAPY OF REFRACTORY EPILEPSY

Tsyvunin V.V., Shtrygol' S.Yu.
National University of Pharmacy, Kharkiv, Ukraine
Department of Pharmacology and Clinical Pharmacy
tsyvunin-vad@ukr.net

Background. One of the possible ways if not to overcome the resistance of refractory epilepsy, then at least to conditionally stable control of seizures due to a decrease in disease activity, can be considered the use in addition to classical antiepileptic drugs (AEDs) medicines from other pharmacological groups – the so-called "non-antiepileptic" drugs. The presence of intrinsic anticonvulsant properties has been established in antiarrhythmic drugs (sodium, potassium and calcium channel blockers, β-adrenergic blockers), cardiac glycosides, arachidonic acid cascade inhibitors (non-steroidal anti-inflammatory drugs, dual inhibitors of COX-2/5-LOX enzymes, leukotriene receptor blockers), antidiabetic drugs (metformin, incretins, inhibitors of sodium-dependent glucose cotransporter type 2), statins, xanthine oxidase inhibitors, etc. However, the ability of these drugs to influence the anticonvulsant potential of classical AEDs has not been studied.

Aim: Experimentally substantiate the use of promising "non-antiepileptic" drugs – cardiac glycosides, inhibitors of sodium-dependent glucose cotransporter 2, dual inhibitors of COX-2/5-LOX enzymes and leukotriene receptor blockers – as adjuvant anticonvulsants to improve pharmacotherapy of refractory epilepsy.

Materials and methods. Various experimental models of acute seizures in mice (pentylenetetrazole-, picrotoxin-, bicuculline-, thiosemicarbazide-, strychnine-, camphor-induced seizures, maximal electroshock) as well as murine model of chronic epileptogenesis – pentylenetetrazole-induced kindling – have been used. For digoxin as the most promising adjuvant, the molecular mechanisms for the implementation of anticonvulsant action *in silico* and *in vivo* have been determined.

Results. The ability of "non-antiepileptic" drugs – cardiac glycoside digoxin, antidiabetic medicine empagliflozin, dual COX-2/5-LOG inhibitor darbufelone and antiallergic drug montelukast – to enhance the anticonvulsant potential of classical AEDs in models of convulsive syndrome with different pathogenesis, especially in situations of incomplete seizure control (equivalent to refractory epilepsy), has been established. The most effective combinations of classical AED sodium valproate with above-mentioned "non-antiepileptic" drugs have been established for the first time. For digoxin its own GABA-ergic properties as well as positive effect on neuroinflammation and neuronal apoptosis have been established. The understanding of the neurochemical mechanisms of the anticonvulsant action of digoxin has been further developed, which allows to improve theoretical knowledge of the pathogenesis of seizures.

Conclusion: Use of "non-antiepileptic" drugs as adjuvant anticonvulsants can be an effective option to improve pharmacotherapy of refractory epilepsy.