

INFLUENCE OF CHRONIC TREATMENT WITH H₁ RECEPTOR ANTAGONISTS ON THE ANTICONVULSANT ACTIVITY OF ANTIEPILEPTIC DRUGS

*Mariusz Świąder¹, Katarzyna Chwalczuk¹, Marian Wielosz¹,
Stanisław J. Czuczwar^{2,3,#}*

¹Department of Pharmacology and Toxicology, ²Department of Pathophysiology, Medical University, PL 20-090 Lublin, Jaczewskiego 8, Poland, ³Isotope Laboratory, Institute of Agricultural Medicine, PL 20-090 Lublin, Jaczewskiego 2, Poland

Influence of chronic treatment with H₁ receptor antagonists on the anti-convulsant activity of antiepileptic drugs. M. ŚWIĄDER, K. CHWALCZUK, M. WIELOSZ, S.J. CZUCZWAR. Pol. J. Pharmacol., 2001, 53, 93–96.

The aim of this study was to evaluate the effects of chronic astemizole and ketotifen administration on the anticonvulsant activity of antiepileptic drugs against maximal electroshock-induced convulsions in mice. Adverse effects were evaluated in the chimney test (motor performance) and passive avoidance task (long-term memory). Brain and plasma levels of antiepileptics were measured by immunofluorescence. Astemizole (2 mg/kg) and ketotifen (8 mg/kg) significantly diminished the electroconvulsive threshold, being without effect upon this parameter at lower doses. Astemizole significantly reduced the anticonvulsant action of phenobarbital and diphenylhydantoin, but it did not affect that of carbamazepine and valproate. Moreover, ketotifen (at the subprotective dose of 4 mg/kg) remained without effect upon the protective activity of valproate, diphenylhydantoin or phenobarbital, but significantly diminished the anticonvulsant effect of carbamazepine. Histamine receptor antagonists combined with antiepileptic drugs, did not alter their brain and free plasma levels. Also, they did not influence adverse potential of carbamazepine, diphenylhydantoin and valproate while that of phenobarbital was significantly enhanced. Valproate, phenobarbital and diphenylhydantoin alone at their ED₅₀s against maximal electroshock or combined with the histamine receptor antagonists disturbed long-term memory. The results of this study indicate that H₁ receptor antagonists, should be used with caution in epileptic patients.

Key words: *astemizole, ketotifen, maximal electroshock, antiepileptic drugs*

[#] *correspondence*; e-mail: czuczwar@galen.imw.lublin.pl