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EFFECT OF ANTIHORMONES IN AMYGDALA-KINDLED SEIZURES IN RATS

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Tamoxifen (TXF; an antiestrogen), cyproterone acetate (CYP; an antiandrogen) and mifepristone (MIF; an antigestagen) did not affect kindling parameters (afterdischarge threshold, seizure severity, seizure duration and afterdischarge duration) in fully-kindled rats. TXF (50 mg/kg) and CYP (50 mg/kg), when combined with carbamazepine, or phenobarbital, both antiepileptics administered at their highest subprotective doses of 15 mg/kg, resulted in significant reduction of the seizure and afterdischarge durations, both in male and female rats. Additionally, the combination of carbamazepine and cyproterone markedly increased the afterdischarge threshold in fully-kindled rats of both genders. The interaction between antihormones and carbamazepine, or phenobarbital, was not reversed by the respective gonadal hormones (estradiol, progesterone, and testosterone), kainic acid, or strychnine. However, the TXF-, and CYP-induced effect on the action of carbamazepine was abolished by bicuculline, N-methyl-D-aspartic acid and aminophylline. The effect of TXF on the protective activity of phenobarbital was reversed by bicuculline and N-methyl-D-aspartic acid. Finally, the CYP-mediated effect on phenobarbital action was abolished by bicuculline and aminophylline. Neither TXF nor CYP altered free plasma levels and brain levels of carbamazepine or phenobarbital, so a pharmacokinetic interaction between antihormones and antiepileptic drugs is not probable. In view of the present data, it may be suggested that the protective activity of the antiestrogen and antiandrogen are mostly associated with the enhancement of GABA-ergic and purinergic transmission in the central nervous system. Also the augmentation of glutamatergic transmission, realized through NMDA receptors, may be involved in the mechanism of antiseizure action of TXF and CYP.

Key words: *antihormones, tamoxifen, cyproterone, antiepileptics, amygdala-kindled seizures*

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