The Synergistic Effect of Raloxifene, Fluoxetine, and Bromocriptine Protects Against Pilocarpine-Induced Status Epilepticus and Temporal Lobe Epilepsy

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The present antiepileptic drugs pose several problems in the management of seizures owing to their meager neuroprotective potential, adverse effects on bone, detrimental effects on cognitive function, chronic toxicity, drug interactions, side effects including aggression, agitation, and irritability and sometimes exacerbation of seizures. We followed up progressive preclinical investigation in mice against pilocarpine (PILO)-induced status epilepticus (SE) and temporal lobe epilepsy (TLE). To determine the response of raloxifene (RF) (4 and 8 mg/kg), fluoxetine (FT) (14 and 22 mg/kg), bromocriptine (BC) (6 and 10 mg/kg), and their low-dose combinations, oral treatment was scheduled for 28 days followed by PILO (300 mg/kg, i.p). The response was stalked for intensive behavioral monitoring of convulsions, hippocampal neuropeptide Y (NPY), and oxidative stress discernment along with histomorphological studies. The resultant data confirmed the therapeutic potential of triple drug combination of raloxifene (4 mg/kg) with fluoxetine (14 mg/kg) and bromocriptine (6 mg/kg) compared to monotherapy with raloxifene (4 mg/kg), and bromocriptine

(6 mg/kg) as otherwise monotherapy with fluoxetine (14 mg/kg) was ineffective to suppress convulsions; an effect better than sodium valproate (300 mg/kg), a standard AED, was validated. Most profoundly, PILO-induced compensatory increases in hippocampal NPY levels (20.01%), which was escalated (100%) with the triple drug combination. The same pattern of results was superseded for oxidative stress indices and neuronal damage. The results for the first time demonstrate the propitious role of triple drug combination in the management of SE and TLE. Therapeutically, this enhancing profile of drugs fosters a safer and more effective drug-combination regimen. [Figure not available: see fulltext.].

Dopamine

Epilepsy

Neurodegeneration

Neuropeptide Y

Serotonin

Status epilepticus

bromocriptine mesilate

diazepam

fluoxetine

neuropeptide Y

pilocarpine

raloxifene

valproic acid

anticonvulsive agent

bromocriptine

fluoxetine

pilocarpine

raloxifene

animal cell

animal experiment

animal model

animal tissue

anticonvulsant activity

Article

controlled study

convulsion

drug efficacy

drug megadose

drug potentiation

drug safety

epileptic state

female

follow up

histopathology

low drug dose

male

monotherapy

mouse

nerve cell lesion

neuroprotection

nonhuman

oxidative stress

pilocarpine-induced seizure

temporal lobe epilepsy

treatment response

animal

chemically induced

combination drug therapy

disease model

drug effect

epileptic state

hippocampus

metabolism

nerve cell

temporal lobe epilepsy

Animals

Anticonvulsants

Bromocriptine

Disease Models, Animal

Drug Synergism

Drug Therapy, Combination

Epilepsy, Temporal Lobe

Female

Fluoxetine

Hippocampus

Male

Mice

Neurons

Oxidative Stress

Pilocarpine

Raloxifene Hydrochloride

Status Epilepticus