Acute treatment with pentoxifylline exerts anti-convulsant effects in pentylenetetrazole-induced seizures of mice: The role of nitric oxide

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Abstract: Pentoxifylline, a nonspecific type 4 phosphodiesterase inhibitor, has proven neuroprotective effects. Studies have shown that pentoxifylline prevents hippocampal neuronal death in the models of epileptic seizures. There is some evidence that nitric oxide pathway is involved in the pentoxifylline action.

We evaluated whether nitrergic system is involved in the anticonvulsant effects of pentoxifylline in a model of clonic seizure in male mice. Materials and methods: Different doses of pentoxifylline were administered intraperitoneally in different groups of mice. L-NAME, a non selective inhibitor of nitric oxide synthase (NOS), aminoguanidine, a selective inhibitor of inducible NOS, 7-NI, a selective inhibitor of neuronal NOS, and L-arginine, a nitric oxide donor were administered to evaluate the role of nitric oxide in pentoxifylline anti-seizure effects. Clonic seizure threshold was determined by infusion of pentylenetetrazole (PTZ, 0.5%) at a constant rate of 1 ml/min into the tail vein of mice (23-29 g). Minimal dose of PTZ to induce clonic seizure was considered as an index of seizure threshold.

Pentoxifylline (150, 200 and 250 mg/kg, 1 h before test) significantly increased the seizure threshold. Acute co-administration of L-NAME (5 mg/kg, i.p.) and 7-NI (40 mg/kg, i.p.) with an effective dose of pentoxifylline (150 mg/kg) inhibited its anticonvulsant effects. Co-administration of aminoguanidine (100 mg/kg, i.p.) with pentoxifylline 150 mg/kg did not alter its anticonvulsant effects. Acute single injection of non-effective dose of L-arginine (60 mg/kg, i.p) with a non-effective dose of pentoxifylline (50 mg/kg) significantly increased the seizure threshold.

Pentoxifylline increases the PTZ-induced clonic seizure threshold in mice. We demonstrated for the first time that nitric oxide signaling probably through neuronal NOS could be involved in the anticonvulsant effects of pentoxifylline.

Keyword: Pentoxifylline, Convulsion, Pentylenetetrazole, Nitric oxide, Mice