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Celecoxib Enhances the Anticonvulsant Effect of Adenosine in an Intravenous Pentylenetetrazole-Induced Seizure Model in Mice

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ABSTRACT

Introduction: As an endogenous neurotransmitter, adenosine has anticonvulsant and neuroprotective effects in the brain. The central effects of adenosine are mediated through A1 and A2A receptors. Activation of the adenosine A2A receptor increases the expression of the cyclooxygenase-2 (COX-2) enzyme. Recent studies have reported that COX-2 inhibitors have anticonvulsant effects. This study aimed to examine the impact of acute adenosine administration, alone or combined with the selective COX-2 inhibitor celecoxib, on pentylenetetrazole-induced clonic and tonic seizure thresholds in mice.

Methods and Materials: NMRI male mice (weighing 25-30 g; n = 10 in each group) were randomly divided into 10 groups, including control, sham (polyethylene glycol 400), and eight experimental groups receiving adenosine (25, 50, and 100 mg/kg), celecoxib (2.5, 5, and 10 mg/kg), pre-treatment with an ineffective dose of celecoxib before ineffective doses of adenosine, and pre-treatment with an effective dose of celecoxib before effective doses of adenosine. Thresholds for the onset of myoclonic twitch (MCT), generalized clonus (GNC), and tonic hindlimb extension (THE) were assessed by intravenous infusion of pentylenetetrazole.

Results: Adenosine at a dose of 50 mg/kg significantly increased the onset of GNC and THE, while a dose of 100 mg/kg significantly increased all seizure endpoints. Celecoxib at a 10 mg/kg dose significantly increased all seizure endpoints. Pre-treatment with celecoxib (5 mg/kg) before adenosine (25 mg/kg) increased only the onset to THE, while pre-treatment with celecoxib (10 mg/kg) before adenosine (100 mg/kg) increased the onset to myoclonic twitch and GNC.

Conclusion and Discussion: Adenosine or celecoxib administration results alone confirm that these compounds have anticonvulsant effects. Potentiating the anticonvulsant impact of adenosine with celecoxib pre-treatment suggests that the effects of adenosine on seizure threshold are partly due to the modulation of the COX-2 pathway.

Keywords: Adenosine, Celecoxib, Cyclooxygenase-2, Pentylenetetrazole, Seizures