Effect of adenosine A1 and A2 receptor stimulation on hypoxia-induced convulsions in adult mice.

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Clinical observations indicate that seizures induced by hypoxia are common kind of convulsive activity in both infants and elderly patients. The occurrence of seizure episode during hypoxia is important risk factor of epilepsy development in the future. Experimental hypoxia was obtained by exposure of adult (20–23 g) Albino Swiss mice to spontaneous breathing in gas mixture composed of 5% oxygen and 95% nitrogen. The latency time to convulsive activity was determined. Single sublethal episode of seizures induced by hypoxia (HS) resulted in higher susceptibility to pentetrazol (PTZ), bicuculline (BCC), N-methyl-D-aspartic acid (NMDA) but not in electrically induced convulsions. Adenosine A1 receptor agonist, R(-)-N6-(2-phenyl-isopropyl)adenosine (R-PIA) (0.01; 0.05; 0.1 mg/kg, ip) prolonged the latency to HS-induced convulsions. A1 receptor antagonist, 8-cyclopentyltheophylline (CPT), reversed the protective action of R-PIA. A2 receptor agonist, N(6)-[2-(3,5-dimethoxyphenyl)-2-(2-methylphenyl)ethyl]adenosine (DPMA), only at the highest dose (5 mg/kg ip) prolonged the latency time to convulsive activity. This effect was only partially reversed by A2 antagonist 3,7-dimethyl-1-propargylxanthine (DMPX). Administered immediately after episode of HS R-PIA diminished the higher susceptibility to PTZ, BCC, NMDA at 3rd day after HS, while DPMA appeared to be ineffective.

These results confirm the important role of adenosine A1 receptor agonist in protection against acute and chronic epileptogenic effect of hypoxia. The role of adenosine A2 receptors seems to be of minor importance.

Key words: adenosine receptors, hypoxia, convulsions