CONTRIBUTION OF THE HISTAMINERGIC RECEPTOR SUBTYPES TO HISTAMINE-INDUCED CEREBELLAR GRANULAR NEUROTOXICITY

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In the present study, we investigated the effects of histamine and its specific H₁, H₂ and H₃ receptor blockers in cerebellar granular cell culture derived from rat pups. Histamine was applied at 10⁻⁹, 10⁻⁸, 10⁻⁷, 10⁻⁶, and 10⁻⁵ M for 16 h into the cultures and the highest dose was found to be the most toxic one. Pheniramine (H₁ receptor blocker), ranitidine (H₂ receptor blocker) and thioperamide (H₃ receptor blocker) were applied at 10⁻⁸, 10⁻⁷, 10⁻⁶, 10⁻⁵ M into the flasks prior to histamine in the second step of the experiments. Also, the effect of all of the blockers together at 10⁻⁵ M concentrations was tested on the toxicity induced by 10⁻⁵ M histamine. The H₃ receptor blocker, thioperamide (10⁻⁶ M) was demonstrated to be most effective histamine toxicity blocker. Histamine H₂ blocker, ranitidine, was found to attenuate histamine neurotoxicity at all doses tested, its most effective dose being the highest dose. On the other hand, H₁ blocker, pheniramine, was able to reverse the effect of histamine at 10⁻⁶ and 10⁻⁵ M, but it was found ineffective when given at 10⁻⁵ and 10⁻⁶ M. Combined application of H₁, H₂, and H₃ receptor blockers at 10⁻⁵ M concentrations, 45 min before histamine addition into the flasks at 10⁻⁵ M, was able to reduce cell death score but it was not as effective as H₃ blocker, thioperamide.

Key words: histamine, neurotoxicity, H₁, H₂, H₃, blocker, cerebellum, cell culture

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