Short communication

Effect of histamine receptor antagonists on aminophylline-induced seizures and lethality in mice

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Abstract:
The aim of this study was to evaluate the effects of H₁ (antazoline and astemizole) or H₂ (cimetidine and famotidine) histamine receptor antagonists on the clonic phase, tonic seizures and mortality of mice challenged with aminophylline to induce convulsions in mice. Moreover, the total plasma and brain concentrations of theophylline were evaluated. Astemizole (1 mg/kg) did not affect the threshold for aminophylline-induced seizures, but when administered at a dose of 2 mg/kg, it significantly reduced the CD₅₀ value of aminophylline from 249 mg/kg to 211 mg/kg (p < 0.01). The remaining histamine receptor antagonists studied i.e., antazoline (up to 1 mg/kg), cimetidine (up to 40 mg/kg) and famotidine (up to 10 mg/kg) had no impact on seizure susceptibility in aminophylline-induced convulsions. Furthermore, astemizole (2 mg/kg) decreased latency to the clonic phase of aminophylline-induced convulsions from 51.1 ± 4.5 to 32.1 ± 4.3 min (p < 0.01). It is noteworthy that astemizole, a novel H₁ receptor antagonist, did not alter the brain and plasma levels of theophylline, so the existence of pharmacokinetic interactions was excluded. Our results indicate that some interactions between methylxanthines and histamine receptor antagonists may be clinically important since these drugs are usually combined during the treatment of status asthmaticus.

Key words:
astemizole, antazoline, cimetidine, famotidine, aminophylline-induced convulsions, mortality