

Protective Effect of Excitatory Amino Acids on Cold-Restraint Stress-Induced Gastric Ulcers in Mice: Role of Cyclic Nucleotides

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摘要

Abstract

Previous studies have shown that excitatory amino acids (EAAs) and their receptors may play important roles in the mammalian enteric system. In this study, we investigated whether EAAs, including l-glutamate (l-Glu) and subtypes N-methyl-d-aspartate (NMDA), kainic acid (KA), and quisqualic acid (QA), reduce cyclic AMP (cAMP) levels and play a role in protecting gastric lesions in cold-restraint stress (CRS) mice. First, we found that dose-dependent administration of four selected EAAs significantly attenuated the increase of cAMP content and exhibited a protective effect on the development of gastric lesions induced by CRS. Second, CRS treatment exhibited a decrease of cGMP content and an increase of cAMP content with marked time-dependent changes, and a high cAMP/cGMP ratio in mice gastric mucosa. Third, pretreatment with 0.25 g/kg or 0.5 g/kg dibutyryl cGMP (db-cGMP) exhibited protective effects on CRS-induced gastric lesions, with preventive ratios of 24.61% and 35.32%, respectively. Moreover, db-cGMP at 0.5 g/kg significantly attenuated the increase in both cAMP content and the cAMP/cGMP ratio in CRS-treated gastric mucosa. In contrast, db-cAMP exhibited no protective effect, and significantly decreased cGMP content and increased the cAMP/cGMP ratio. These results suggest that EAAs significantly reduce CRS-induced gastric ulcers in mice. The possible mechanism of the antiulcer activity of EAAs may be related to a decrease in the cAMP content in the gastric mucosa of mice. In addition, an increase of the cAMP/cGMP ratio significantly involved in CRS-induced gastric ulcer formation in mice