Evidence for the gastric cytoprotective effect of centrally injected agmatine.

Abstract:

Agmatine (decarboxylated arginine) exerts cytoprotective action in several tissues, such as in the brain, heart or kidneys, but there is still controversy over the effects of agmatine on the gastric mucosa. The aim of the present study was to reveal the potential gastroprotective action of agmatine by using an acid-independent ulcer model to clarify which receptors and peripheral factors are involved in it. Gastric mucosal damage was induced by acidified ethanol. Mucosal levels of calcitonin gene-related peptide (CGRP) and somatostatin were determined by radioimmunoassay. For analysis of gastric motor activity the rubber balloon method was used. It was found that agmatine given intracerebroventricularly (i.c.v., 0.044-220 nmol/rat) significantly inhibited the development of ethanol-induced mucosal damage, while in the case of intraperitoneal injection (0.001-50mg/kg i.p.) it had only a minor effect. The central gastroprotective action of agmatine was completely antagonized by mixed alpha2-adrenoceptor and imidazoline I1 receptor antagonists (idazoxan, efaroxan), but only partially by yohimbine (selective alpha2-adrenoceptor antagonist) and AGN 192403 (selective I1 receptor ligand, putative antagonist). It was also inhibited by the non-selective opioid-receptor antagonist naloxone and the selective ?-opioid receptor antagonist naltrindole, but not by ?-funaltrexamine and
nor-Binaltorphimine (selective ?- and ?-opioid receptor antagonists, respectively). Furthermore, the effect of agmatine was antagonized by bilateral cervical vagotomy and by pretreatment with indomethacin and NG-nitro-l-arginine. Agmatine also reversed the ethanol-induced reduction of gastric mucosal CGRP and somatostatin content, but did not have any significant effect on gastric motor activity. These results indicate that agmatine given centrally induces gastric cytoprotection, which is mediated by central imidazoline I1 receptors, alpha2-adrenoceptors and ?-opioid receptors. Activation of these receptors induces the release of different mucosal protective factors, such as NO, prostaglandins, CGRP and somatostatin by a vagal-dependent mechanism. Alterations of gastric motility are not likely to contribute to the observed protective effect.