Neuropeptide S reduces duodenal bicarbonate secretion and ethanol-induced increases in duodenal motility in rats

Abstract

Alcohol disrupts the intestinal mucosal barrier by inducing metabolic and functional changes in epithelial cells. Recently, we showed that neuropeptide S (NPS) decreases duodenal motility and increases mucosal paracellular permeability, suggesting a role of NPS in the pathogenesis of disorders and dysfunctions in the small intestine. The aim of the present study was to investigate the effects of NPS on ethanol- and HCl-induced changes of duodenal mucosal barrier function and motility. Rats were anaesthetized with thiobarbiturate, and a 30-mm segment of the proximal duodenum with an intact blood supply was perfused in situ. The effects on duodenal bicarbonate secretion, the blood-to-lumen clearance of 51Cr-EDTA, motility and transepithelial net fluid flux were investigated. Intravenous (i.v.) administration of NPS significantly reduced duodenal mucosal bicarbonate secretion and stimulated mucosal transepithelial fluid absorption, mechanisms dependent on nitrergic signaling. NPS dose-dependently reduced ethanol-induced increases in duodenal motility. NPS (83 pmol·kg-1·min-1, i.v.) reduced the bicarbonate and fluid secretory response to luminal ethanol, whereas a 10-fold higher dose stimulated fluid secretion but did not influence bicarbonate secretion. In NPS-treated animals, duodenal perfusion of acid (pH 3) induced greater bicarbonate secretory rates than in controls. Pre-treating animals with N?-nitro-L-arginine methyl ester (L-NAME) inhibited the effect of NPS on bicarbonate secretion. In response to luminal acid, NPS-treated animals had significantly higher paracellular permeability compared to controls, an effect that was abolished by L-NAME. Our findings demonstrate that NPS reduces basal and ethanol-induced increases in duodenal motility. In addition, NPS increases luminal alkalinization and mucosal permeability in response to luminal acid via mechanisms that are dependent on nitric oxide signaling. The data support a role for NPS in neurohumoral regulation of duodenal mucosal barrier function and motility.