Ghrelin improves lipopolysaccharide-induced gastrointestinal motility disturbances: roles of nitric oxide and prostaglandin E2

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摘要

Abstract

Ghrelin, an important orexigenic peptide, exerts gastroprokinetic and anti-inflammatory effects. We investigated the role of ghrelin in LPS-induced gastrointestinal (GI) motility disturbances through NO and prostaglandin E2 pathways in mice. Ghrelin-containing cells and its receptor, growth hormone secretagogue receptor 1 (GHSR-1), were localized in the stomach and duodenum using an immunohistochemical method. The distribution of ghrelin-containing cells or GHSR-1 immunoreactivity in both the mucosal and the muscle layers was heterogeneous within both tissues. The i.p. administration of ghrelin (1-20 microg/kg) had no effect on gastric emptying but markedly increased the GI transit (GIT) in normal mice. LPS (20 mg/kg i.p.)-treated mice showed significant decreases in the gastric emptying and GIT. Ghrelin attenuated the LPS-induced delay in gastric emptying and GIT. We also performed immunohistochemical experiments on both tissues. Immunohistochemistry showed the presence of iNOS and cyclooxygenase 2 in both tissues of LPS-treated mice. Treatment of LPS-exposed mice with ghrelin (20 microg/kg) diminished the presence of iNOS but not cyclooxygenase 2 in both tissues. The effect of ghrelin on regulating LPS-induced GI motility disturbance was further found to be associated with a reduction in iNOS expression in the GI tract and plasma NO overproduction rather than regulation of neural or endothelial NO synthase expression in the GI tissue. In addition, ghrelin was found to elevate prostaglandin E2 levels in the GI tissue but showed no significant change in LPS-treated mice. These findings indicate that the action of ghrelin binding to GHSR-1 improves endotoxemia-induced GI motility disturbances mainly through down-regulating the NO pathway in the GI tract.