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Relaxin and gastrointestinal motility

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Summary

Relaxin is involved in a variety of functions. Among them, relaxin influences gastrointestinal motility in mice mainly regulating the biosynthesis of nitric oxide, considered as the main substance causing smooth muscle relaxations. Relaxin is able to regulate the different nitric oxide synthase expression depending on the gut region considered. Relaxin also counteracts the hypermotility state, related to a defective nitric oxide production, observed in the gut of dystrophic (mdx) mice.
From the above considerations, it appears that relaxin, in addition to its physiological roles, may be regarded as a therapeutic tool in gastrointestinal diseases characterized pathogenically by an altered nitric oxide production.

Key words

Relaxin, nitric oxide; gastrointestinal motility

The possibility that relaxin (RLX) might be involved in the control of gastrointestinal motility by regulating nitric oxide (NO) biosynthesis, as it does in other smooth muscle target organs (3), was investigated.

Mechanical experiments have shown that RLX influenced gastrointestinal motility in female mice through a NO-mediated mechanism acting at the neurotransmission or at the muscular level depending on the gut segment considered (1,2,4). In agreement, immunohistochemical results, showed that RLX regulates, in a selective manner, the expression of the different nitric oxide synthase (NOS) isoforms (Table 1). RLX-induced decrease of small bowel motility may play a physiological role during pregnancy directed to increase the intestinal transit time, so favoring the absorption of nutrients. The increased contractile activity of the colonic muscle by RLX could be aimed at facilitating absorption of a major quantity of water by a continuous mixing of the content, so contributing to constipation, the main symptom in pregnancy.

Besides its physiological role, the possibility that RLX may also have some beneficial effects in those gastrointestinal motor alterations related to a defective NO production, such as those reported in the dystrophic (mdx) mice, was investigated.

Functional experiments showed that RLX was able, through a NO-mediated mechanism, to reverse the altered gastrointestinal motor responses in preparations from mdx male mice (1,4). Of note, in mdx mice, the hormone appeared to compensate for the NO defect until a normal motility has been restored. In keeping, immunohistochemical experiments showed that RLX up-regulated the expression of only

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those NOS that resulted defective in the mdx preparations (i.e. nNOS and iNOS in gastric and ileal preparations, respectively) .

Table 1. Modulation of NO generation by RLX in the gastrointestinal tract of mice

Gatrointestinal tract	Model	Evidence for NO production	NO synthase regulation	Biological effects
Gastric fundus	ex vivo in vivo	NOS inhibition (L-NNA)	nNOS (protein) eNOS (protein)	Decreased motility, normalization of hypermotility
Ileum	ex vivo in vivo	NOS inhibition (L-NNA)	iNOS (protein) eNOS (protein)	Decreased motility, normalization of hypermotility
Proximal colon	ex vivo	NOS inhibition (L-NNA)	nNOSß (protein) nNOSα (protein) eNOS (protein)	Decreased basal tension, increased spontaneous contractions

In conclusion, RLX influences gastrointestinal motility mainly regulating, in a selective manner, the expression of the different NOS isoforms. Thus, even though caution is needed in extrapolating data obtained in animals to humans, may be regarded as a potential tool in the therapeutic approach to gastrointestinal motor disorders caused by altered NO production.

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