# Effect of Propranolol on Duodenogastric Dyskinesia Induced by Ulcerogenic Activity of Pentagastrin

K. A. Shemerovskii

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Gastrin is one of the factors in ulcerogenesis [3-5,7,8,15], although its role in ulcer production is difficult to explain by invoking secretory mechanisms alone. The gastrin-induced alteration in gastric motor function precedes the secretory responses, and myocytes are more sensitive to this peptide than are epitheliocytes [4,6,11]. Pentagastrin may both stimulate and inhibit the motor and myoelectrical activities of the stomach and intestine [1,2,11,12,14], but it has not been fully elucidated what contribution adrenergic mechanisms make to the action of gastrin on gastrointestinal motor function [1,13,14]. The purpose of the present study was to examine how blockade of β-adrenergic receptors might affect the duodenogastric dyskinesia induced by ulcerogenic doses of pentagastrin.

## MATERIALS AND METHODS

Chronic tests were carried out on 5 male rabbits 2.8-3.7 kg in weight in which, 1-2 weeks before the tests, looped electrodes were implanted into smooth muscles of the stomach, pyloric sphincter, and duodenum as described previously [9,10]. Activities of the gastric, pyloric, and duodenal smooth muscles were recorded on an encephalograph at a rate of 7.5 mm/sec at a time constant of 0.3. The rabbits were fed the standard diet (oats, vegetables, hay). The tests were run from 10:00 to 14:00 h without imposing any dietary restrictions on the animals. In the first series of tests, ulcerogenic doses of pentagastrin [4,8] were injected subcutaneously at 0.2 mg/kg daily for 5 days. In the second series, the β-blocker propranolol was injected intravenously at 2 mg/kg 10-20 min before pentagastrin. One hour before and one hour after pentagastrin injection, the frequency of bursts of action potentials was determined. The magnitude of pentagastrin activity was analyzed in detail both before and after the beta blockade, particularly during the first 10 min of its effect (the start of pentagastrin action) and during the last 10 min (the end of pentagastrin action). The statistical significance of differences between mean values was evaluated by the range of their variation (at the 95% level of significance).

## RESULTS

The subcutaneous injection of pentagastrin elicited, in each rabbit, a triphasic reaction of myoelectrical activity in the gastroduodenal zone (Fig. 1). The first (inhibitory) phase of this reaction was characterized by a short-term (1-3 min) discontinuation of action potentials in all three electromyograms. The second (tachygastric) phase was marked by an increased frequency (for 4-12 min) of action potential bursts recorded from the stomach and pyloric sphincter, whereas the duodenal

Department for Visceral Systems Physiology, Research Institute of Experimental Medicine, Russian Academy of Medical Sciences, St. Petersburg. (Presented by B. I. Tkachenko, Member of the Russian Academy of Medical Sciences)

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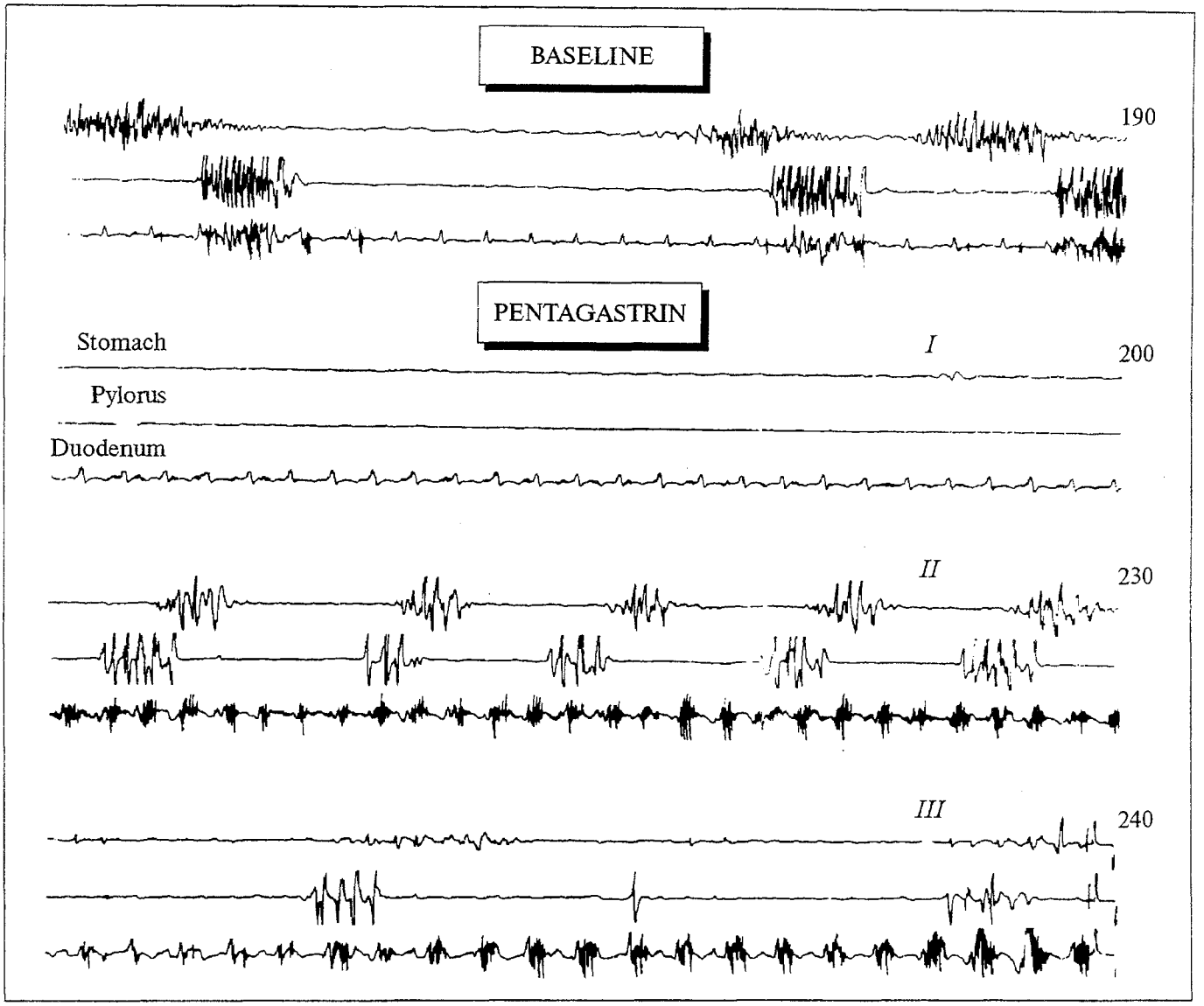


Fig. 1. Triphasic reaction of myeloelectrical activity in the gastroduodenal zone to subcutaneous injection of pentagastrin.

activity remained normal. The third phase of pentagastrin action was characterized by weakened gastric and sphincteric activities and intensified duodenal activity for 40-50 min. Under the action

TABLE 1. Effect of Pentagastrin on Myoelectrical Activity of Gastroduodenal Zone in Rabbits with Blocked b-Adrenergic Receptors. The Values are Means±SEM ($n=5$)

| Drug | Frequency of action potential bursts, $min^{-1}$ | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | baseline | | | start of pentagastrin action | | | end of pentagastrin action | | |
| | stomach | pylorus | duodenum | stomach | pylorus | duodenum | stomach | pylorus | duodenum |
| Pentagastrin, 0.2 mg/kg | 2.9±0.3 | 2.0±0.3 | 13.2±1.9 | 3.2±0.8 (+10%) | 3.0±1.0* (+50%) | 21.0±1.0 (+59%) | 1.7±0.5* (−41%) | 1.5±0.5 (−25%) | 20.8±1.0* (+57%) |
| Propranolol, 2 mg/kg | 2.6±0.1 | 1.9±0.2 | 14.6±2.1 | 2.9±1,3 | 2.5±0.8 | 14.2±5.1 | 2.2±0.5 | 2.2±1.0 | 11.6±2.0 |
| Propranolol + pentagastrin | 2.5±0.2 | 2.1±0.3 | 10.5±1.7 | 3.5±1.5 (+40%) | 3.3±1.5* (+57%) | 19.2±3.6* (+83%) | 1.3±0.3* (−48%) | 1.3±0.3* (−38%) | 15.6±5.6* (+48%) |

Note. The asterisk indicates a significant difference ($p<0.05$) relative to the baseline.

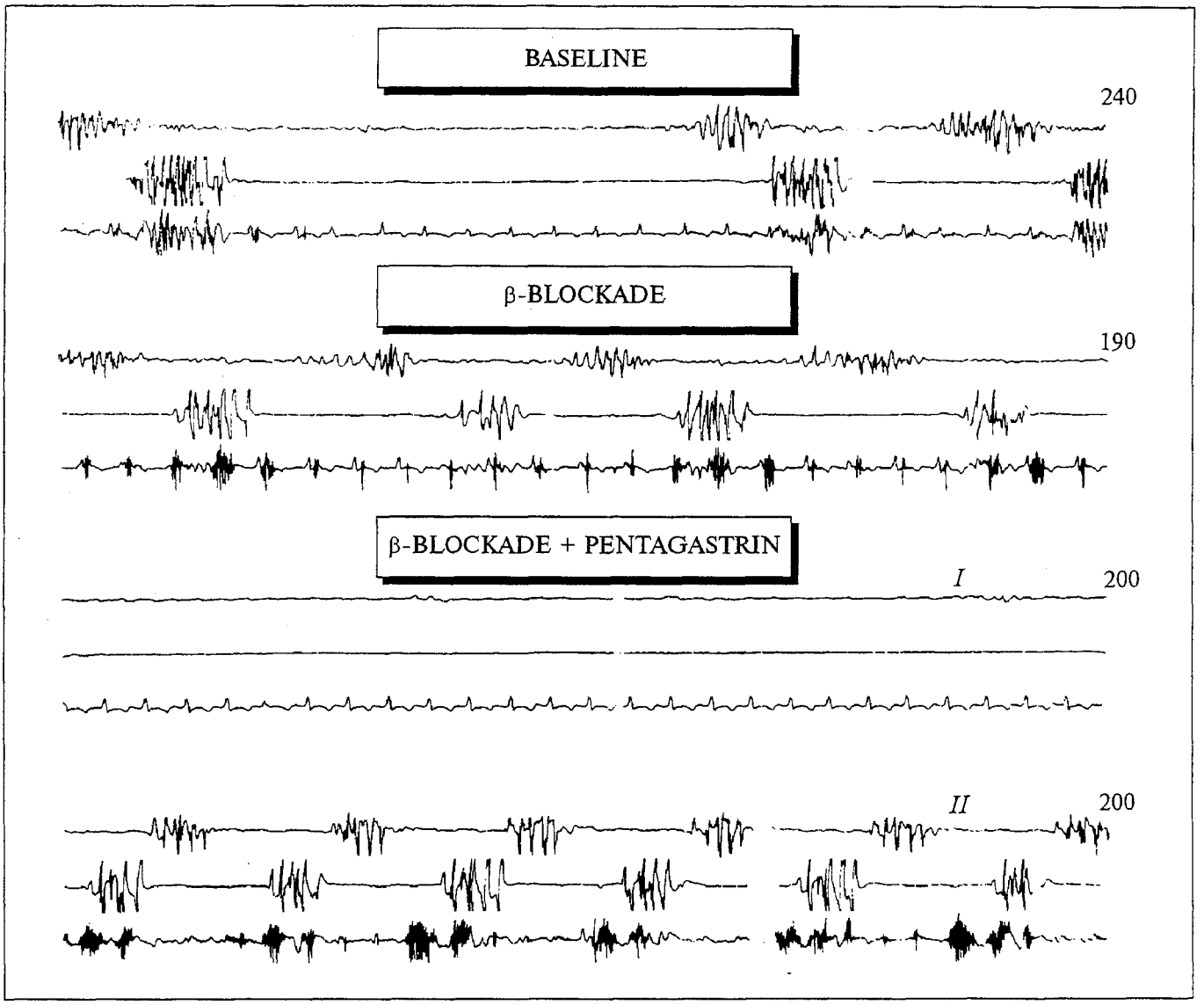


Fig. 2. Short-term increase in the frequency of action potential bursts in the gastroduodenal zone caused by propranolol.

of pentagastrin, therefore, the activity of the duodenal muscles eventually came to predominate over those of the pyloric and gastric muscles.

As shown in Table 1, whereas all three areas of the gastropyloroduodenal zone were activated in the early period of pentagastrin action (during the first 10 min of its effect), the gastric and sphincteric activities were weakened but the activity of the duodenum was increased at the end of pentagastrin action (during the last 10 min of its effect). Such a lack of correspondence between the duodenal and gastric activities is an indication of duodenogastric dyskinesia.

The observed bilateral duodenogastric dyskinesia induced by pentagastrin indicates that one possible mechanism of the ulcerogenic action of gastrin may be a duodenogastric reflux at the basis of which is bilateral duodenogastric dyskinesia.

The intravenous injection of propranolol (2 mg/kg) resulted in a brief (for 2-5 min) increase in the frequency of action potential bursts in the gastroduodenal zone (Fig. 2). A statistical analysis of the effect of propranolol (Table 1) showed that these changes were insignificant over a longer period (10 min), both at the start and at the end of the tests. On the other hand, the propranolol-induced bradycardia was significant throughout the observation period. Consequently, the beta blockade did not alter coordinated activity of the smooth muscles.

When pentagastrin was injected after the beta blockade by propranolol, an inhibitory and, predominantly, a tachygastric phase of its action was observed (Fig. 2). The tachygastria was of a dyskinetic type since action potential bursts occurred in the electroduodenogram earlier than they

did on the electropylogram and especially on the electrogastrogram. Under these conditions, therefore, pentagastrin could induce a retrograde duodenogastric dyskinesia.

Thus, the blocking of β-adrenoreceptors with propranolol, without eliminating the pentagastrin-induced duodenogastric dyskinesia, only modified it somewhat (from a bilateral to a retrograde variety).

As shown by the statistical analysis (Table 1), both before and after the beta blockade, the activity of all three areas of the gastroduodenal zone was stimulated by pentagastrin at the beginning of its action, whereas it stimulated only the duodenal muscles and weakened the activity of the pyloric and gastric muscles at the end of its action.

In summary, this study indicates that ulcerogenic doses of pentagastrin lead to a bilateral duodenogastric dyskinesia which, far from being eliminated by the blockade of β-adrenergic receptors with propranolol, becomes transformed into a retrograde duodenogastric dyskinesia.

The finding that pentagastrin led to a more strongly marked (retrograde) dyskinesia after the beta blockade than before it (when only a relative bilateral dyskinesia was observed) suggests that adrenergic mechanisms may be directed at preventing the aggravation of duodenogastric dyskinesia.

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