EFFECT OF PROPRANOLOL ON GASTRODUODENAL MYOELECTRICAL ACTIVITY

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Catecholamines are known to induce membrane hyperpolarization of myocytes, to reduce their spontaneous activity and excitability, to relax intestinal muscles, and to inhibit secretion of acetylcholine, a regulator of intestinal contractions [1-9, 11]. The relaxing effect of catecholamines relative to the motor function of the digestive tract suggests that they may be regarded as "relaxation regulators" [5, 13, 14]. Meanwhile, the problem of the effect of β-adrenoreceptor blockade on motor function of the gastrointestinal tract has not yet been completely explained. On the one hand [9], β-adrenoreceptor blockade increased motor activity of the small intestine (by 34%), but on the other hand, it had no significant effect on electrical activity of the stomach and intestine [3, 13] or likewise on peptide-induced contractions of the gastrointestinal tract [5].

The aim of this investigation was to study electrical activity of smooth muscles of the stomach, pyloric sphincter, and duodenum before and after β-adrenoreceptor blockade by propranolol (Obsidan), injected intravenously into conscious rabbits under conditions as close to physiological as possible.

EXPERIMENTAL METHOD

Chronic experiments were carried out on 14 male rabbits weighing 2.5-3.5 kg. Under sterile conditions silver loop electrodes were implanted in the smooth muscles of the body of the stomach, pyloric sphincter, and duodenum by the method of Papasova and Milenov [12, 13], in our modification [11], 1-2 weeks before the experiment. The electrodes were implanted by a bipolar technique. The distance between individual electrodes in each of the three pairs was 5-10 r distance between the pairs of electrodes was 3-6 cm. Activity of smooth muscles of the gastropyloroduodenal recorded on an encephalograph (recording speed 7.5 mm/sec, time constant 0.3). The rabbits were given an ordinary (vegetables, oats, hay). The animals were taken from the animal house for the experiment starting from 10 a.m. without any preliminary dietary restrictions. Altogether there were 67 experiments. Before the beginning of each experiment a polyethylene catheter was inserted into the marginal vein of the rabbit's ear in order to allow remote intravenous injection of Obsidan without producing recording artefacts of any kind during bolus injection. The injection was given slowly (over a period of 1-2 min). For β-adrenoreceptor blockade [3, 9, 13] propranolol hydrochloride (Obsidan, East Germany) was injected intravenously into the rabbits in the form of a 0.1-5.0% solution in doses of 0.4, 1.0, and 2.0 mg/kg daily for 5 days. The duration and intensity of the changes in muscle electrical activity in the stomach, pylorus, and duodenum were analyzed on the basis of the character and frequency of bursts of action potentials. The statistical significance of the differences in the mean values was determined on the basis of their confidence intervals at a 95% level of significance.

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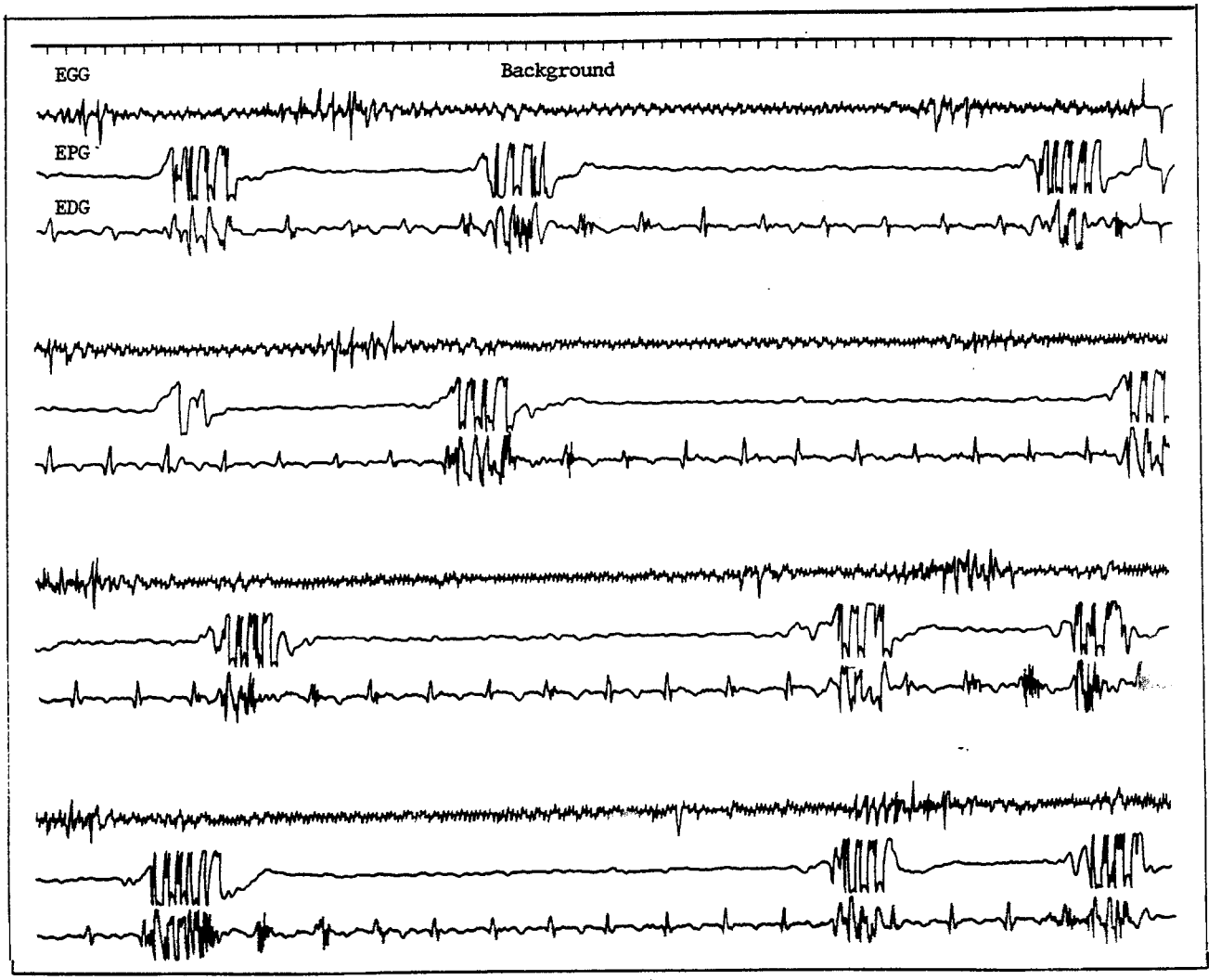

Fig. 1. Myoelectrical activity of gastroduodenal zone before injection of propranolol. EGG) electrogastrogram, EPG) electropylorogram; EDG) electroduodenogram. Fragments of electromyograms at 1st, 2nd, 10th, and 50th minutes. Time marker 1 sec; calibration 500 μV.

EXPERIMENTAL RESULTS

Electrical activity of smooth muscles of the gastroduodenal zone before injection of propranolol is illustrated in Fig. 1. In each of the four fragments of electromyograms (at the 1st, 2nd, 10th, and 50th minutes of recording), illustrating spontaneous myoelectrical activity, the frequency of bursts of action potentials in the stomach corresponded to that for the pyloric sphincter, and also for the frequency of appearance of groups of bursts of duodenal action potentials. The frequency of the coordinated bursts of action potentials in the gastroduodenal zone before injection of propranolol varied within the range 2.5-3.0 per minute.

Besides a constant negative chronotropic effect on the heart, intravenous injection of propranolol as a rule induced either a weak or a well marked biphasic change in the myoelectrical activity of the gastroduodenal zone. Propranolol, in a dose of 0.4 mg/kg, caused slowing of the rhythm of the electrocardiograms, and the bradycardic effect reached almost 10% of the spontaneous heart rate. This minimal dose of propranolol (0.4 mg/kg) caused not always reproducible changes in myoelectrical activity of the gastroduodenal zone. Comparison of the cardiotropic and gastrotropic effects of propranolol demonstrates, evidently, the greater sensitivity of the myocardium compared with that of the gastric muscles to propranolol, when injected in minimally effective doses.

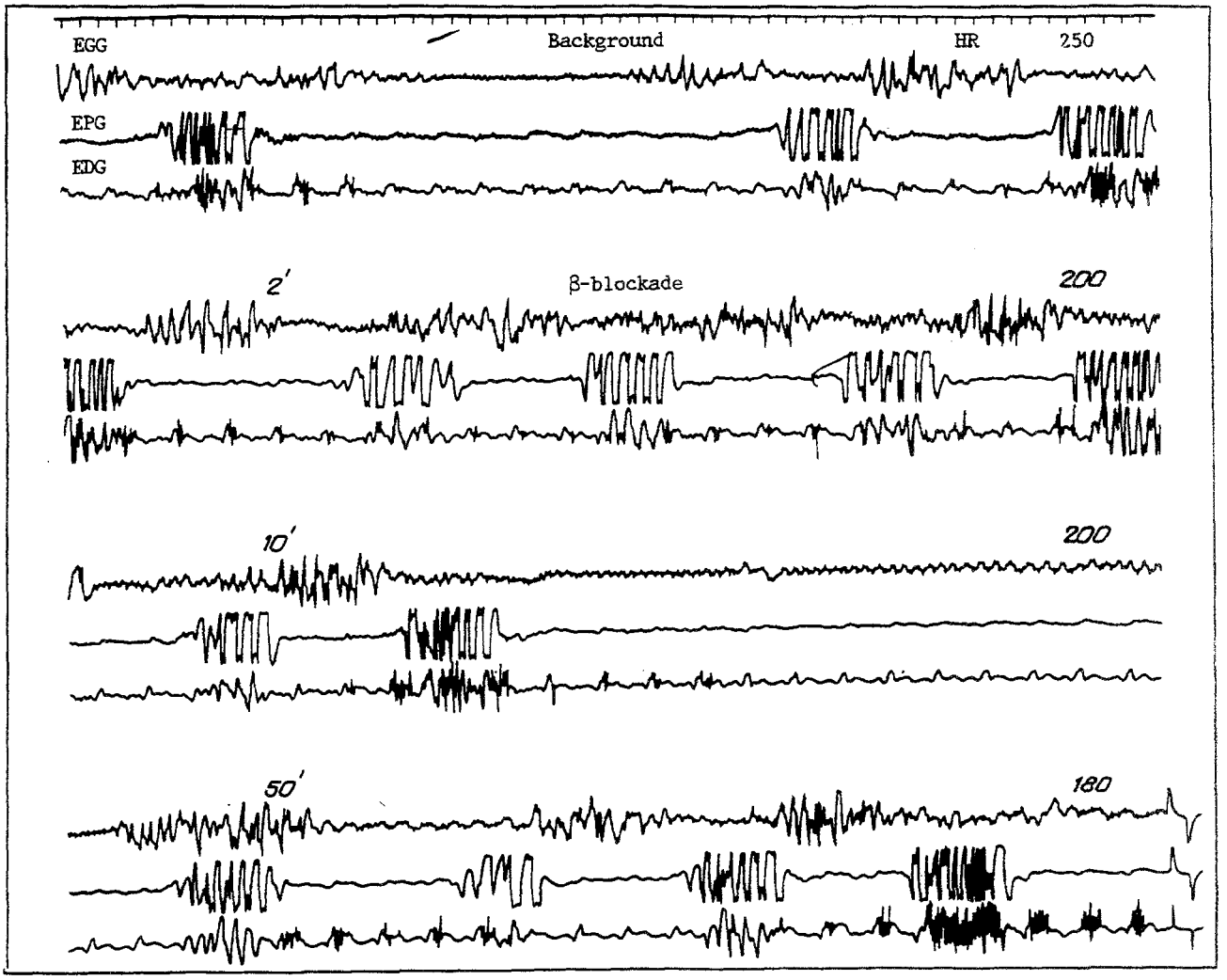

Fig. 2. Myoelectrical activity of gastroduodenal zone before and after injection of propranolol. Above – spontaneous activity. Next – activity of stomach (EGG), pylorus (EPG), and duodenum (EDG) at 2nd, 10th, and 50th minutes after intravenous injection of propranolol (2 mg/kg). Numbers on the right indicate frequency of electrocardiograms.

Propranolol in a dose of 1 mg/kg led to a constant decrease in frequency of the electrocardiograms; the bradycardic effect, moreover, was greater and reached almost 14%. Meanwhile, under the influence of this dose of propranolol the maximal increase in frequency of bursts of action potentials in the gastroduodenal zone (from 2.6 ± 0.3 to 3.4 ± 0.4) reached 30%. Comparison of these cardiotropic and gastrotropic effects indicates that the reactivity of the gastric muscles (to propranolol) is almost twice as high as the reactivity of the myocardium (14 and 30%).

Increasing the dose of propranolol to 2 mg/kg, which is considered to be the most effective dose [2, 3, 13, 15], led to an even greater fall of frequency of the electrocardiograms; the bradycardia reached 23% and was observed for longer than 1 h. This dose of propranolol led to a simultaneous increase in frequency of the bursts of action potentials in the gastroduodenal zone by 66% (on average from 2.6 ± 0.3 to 4.3 ± 0.4 bursts per minute). Comparison of the bradycardic and tachygastric effects (23% and 66%) confirmed the greater reactivity of the gastric muscles than of the myocardium to propranolol.

An increase in the frequency of bursts of action potentials appearing on the gastroduodenomyograms under the influence of propranolol was characteristic chiefly of the first phase of its action, and it lasted for 2-5 min. The fragment of the electromyograms of the stomach, pyloric sphincter, and duodenum at the second minute after injection of propranolol is shown in Fig. 2. The second phase of the action of propranolol, illustrated in Fig. 2 by fragments of the recording at the 10th and 5th minutes, manifested itself as a frequent alternation of lowering (to 33%) and subsequent rising (to 33%) of

the frequency of bursts of action potentials in the gastroduodenal zone in the course of 1 h in the presence of relatively constant bradycardia, in the form of a decrease of almost 23% in the heart rate.

This character of change in the myoelectrical activity of the gastroduodenal zone under the influence of propranolol suggests activation (as a result of β-adrenoreceptor blockade) of the mechanism of so-called "oscillatory autoregulation" of gastric muscular activity, which is responsible for the cyclic pattern of altered gastroduodenal motor function.

This mechanism of "oscillatory autoregulation" evidently reflects periodic adaptation to changes in the level of adrenergic activity inherent in intestinal myocytes (which possess marked self-regulating activity).

The marked reactivity of the gastroduodenal muscles (toward β-adrenergic blockade), manifested during the first phase of the action of propranolol, as well as involvement of the mechanism of "oscillatory autoregulation" of their activity (during the second phase of action of propranolol), are thus evidence of the essential role of β-adrenoreceptor blockade in activity of the gastroduodenal muscles and, consequently, of the important physiological role of the level of β-adrenergic activity in the mechanism of regulation of gastroduodenal myoelectrical activity.

LITERATURE CITED

1. O. M. Avakyan, Pharmacologic Regulation of Adrenoreceptor Function [in Russian], Moscow (1988).
2. S. V. Anichkov, Neuropharmacology [in Russian], Leningrad (1982).
3. E. S. Atanasova, The Intramural Nervous System and Gastrointestinal Motor Function [in Bulgarian], Sofia (1981).
4. R. Blattner, H. Classen, H. Deinert, and H. Doering, Experiments on Isolated Smooth Muscle Preparations [Russian translation], Moscow (1983).
5. V. T. Ivashkin, V. Yu. Vasil'ev, and E. S. Severin, Levels of Regulation of the Functional Activity of Organs and Tissues [in Russian], Leningrad (1987).
6. G. F. Korot'ko, Introduction to Physiology of the Gastrointestinal Tract [in Russian], Tashkent (1987).
7. R. S. Orlov, in: Textbook of Physiology. Physiology of the Autonomic Nervous System [in Russian], Moscow (1987).
8. P. V. Sergeev and N. L. Shimanovskii, Rceptors of Physiologically Active Substances [in Russian], Moscow (1987).
9. A. V. Frol'kis, Pharmacologic Regulation of Intestinal Function [in Russian], Leningrad (1981).
10. K. A. Shemerovskii, Byull. Éksp. Biol. Med., No. 10, 394 (1978).
11. M. F. Shuba, in: Textbook of Physiology. Physiology of the Autonomic Nervous System [in Russian], Leningrad (1981).
12. M. Papasova and K. Milenov, Bull. Inst. Physiol., No. 9, 187 (1965).
13. M. Papasova, V. Velkova, and E. Atanassova, Acta Physiol. Pharmacol. Bulg, **5**, No. 2, 3 (1979).
14. D. J. Leshman, M. R. Anderson, and G. M. Lees, Regul. Peptides, **22**, No. 4, 415 (1988).
15. G. J. Grover, H. R. Weiss, and J. B. Kostis, Eur. J. Pharmacol., **142**, 103 (1987).