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EFFECT OF PENTACTASTRIN AND SUBSTANCE P ON PARIETAL GASTRIC GLANDULOCYTES

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UDC 612.323:612.343

KEY WORDS: pentagastrin; substance P; gastric secretion; glandulocytes; acetylcholinesterase

Endogenous and exogenous peptides, circulating in the blood stream, have both direct and indirect action on effector cells. In the latter case the effect of the peptides is linked with their action on the sympathetic and parasympathetic nervous system [9, 10], while their direct action is due to interaction of their molecules with specific receptors [1, 6-8, 11]; primary binding of peptides with the lipid matrix of the membranes has been postulated [3, 4]. There is evidence in the literature of a mediator role of peptides for the metasympathetic nervous system [2], on the effect of peptides on effector cells through cholinergic pathways (acetylcholine receptors), and on the leading role of peptides in adrenergic mechanisms of regulation of the functions of the body under physiological and pathological conditions [5].

This polarity of views on the ways of interaction of peptides with effector cells motivated the study of the effect of the peptides pentagastrin and substance P on the secretory cells of the stomach. The aim of this investigation was to study the effect of these peptides on secretion of gastric juice and acid production by the parietal glandulocytes of the dog's stomach.

EXPERIMENTAL METHOD

The effect of pentagastrin (6 μg/kg), substance P (2.5, 5, and 10 g/kg), and the acetylcholinesterase blocker calimin (0.2 μg/kg), injected subcutaneously, on the secretion of gastric juice was studied in chronic experiments on dogs with a gastric fistula [1]. Total acidity, free hydrochloric acid, and the rate of its production, were determined in the gastric juice.

EXPERIMENTAL RESULTS

As Fig. 1a, b shows, subcutaneous injection of pentagastrin stimulates the secretion of gastric juice and of free hydrochloric acid by the parietal glandulocytes of the stomach, which was recorded reliably during the first 10 min after injection of pentagastrin. The volume of juice and concentration of free hydrochloric acid in it increased during the next 40 min (the peak of secretion), after which these parameters of gastric secretion declined until 90 min (Fig. 1a). During acetylcholinesterase blockade by calimin, against the background of pentagastrin-induced gastric secretion, potentiation of the secretion of gastric juice and of free HCl production was observed (Fig. 1b). The total volume of gastric juice and the duration of gastric secretion in this case both were increased by 2-2.5 times, and gastric secretion and free HCl production reached their peak values 10-15 min earlier than in the absence of calimin.

Laboratory of Membranology, Research Institute of Physiology, T. G. Shevchenko Kiev University. (Presented by Academician of the Russian Academy of Medical Sciences I. P. Ashmarin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 114, No. 11, pp. 466-467, November, 1992. Original article submitted April 23, 1992.

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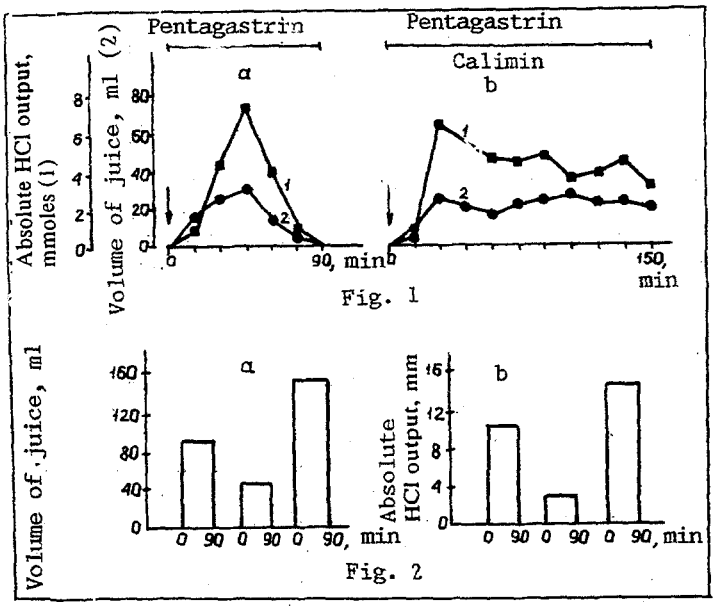

Fig. 1. Effect of pentagastrin (a) and of calimin and pentagastrin (b) on gastric secretion.

Fig. 2. Effect of substance P (b), of calimin and substance P (c), on gastric secretion induced by pentagastrin (a).

TABLE 1. Effect of Substance P on Gastric Secretion Evoked by Pentagastrin in Dogs (M ± m, n = 10)

Parameters of secretion	Pentagastrin, 6 μg/kg	Substance P (2.5 μg/kg) preceded by pentagastrin
Volume of gastric juice, ml	97,4±9,1*	44,2±8,2*
Absolute total acidity, mM	12,1±1,0*	4,9±0,9*
Absolute free hydrochloric acid, mM	10,3±0,8*	3,5±0,5*

Legend. Asterisk indicates values differing significantly from control ($p < 0.05$).

The results of these experiments show that blocking acetylcholinesterase by calimin promotes the cholinergic influence of pentagastrin on secretion of the parietal glandulocytes of the canine stomach.

In the next series of experiments gastric secretion stimulated by pentagastrin (control) and secretion stimulated simultaneously by pentagastrin and substance P was investigated. Table 1 shows that substance P strongly inhibited pentagastrin-induced secretion of gastric juice and also reduced production of total acidity and of free HCl. For instance, during the period of the stimulating effect of pentagastrin on gastric secretion (90 min) the total volume of gastric juice fell by 54.6%, the absolute total acidity fell by 59.5%, and the absolute free HCl by 64%. A further increase in the dose of this peptide (over 5 μg/kg) did not cause any progressive decrease either in the volume of gastric juice or in its acidity.

To analyze the inhibitory action of substance P on pentagastrin-induced gastric secretion, experiments were carried out with calimin. As Fig. 2 shows, substance P has an inhibitory effect on "pentagastrin" secretion. Calimin not only prevents the inhibitory effect of substance P on pentagastrin-induced gastric secretion (Fig. 2c), but also restores it. The parameters of gastric secretion under these circumstances were actually increased by 10-15%. The restoration and enhancement of these parameters of pentagastric gastric secretion in the presence of substance P

(volume of gastric juice, lowering of the free HCl level) can probably be explained by blocking of acetylcholinesterase by calimin, as we observed also in experiments in which pentagastrin alone was given (Fig. 1b).

These experiments with pentagastrin, substance P, and calimin thus demonstrate the involvement of the peptides studied in the cholinergic processes of gastric juice secretion and free HCl production by the parietal glandulocytes of the dog's stomach. These findings are in agreement with those published by other workers [10, 11] on the effect of substance P on contraction of the myocytes of the gastrointestinal tract and participation of this peptide in the stimulation of cholinergic neurons.

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