Effects of Calcium Ions on Electrical Responses of Gastric Gland Cells to Histamine and Pentagastrin

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Abstract. The effect of Ca ions on electrical responses of gastric gland cells on histamine and pentagastrin was investigated using intracellular glass microelectrodes. It was established that in low-calcium solutions hyperpolarization induced by these secretagogues was diminished. In calcium-free solutions and in solutions with blockers of the calcium current hyperpolarization induced by histamine and pentagastrin was not observed. It was suggested that external calcium ions are necessary for hyperpolarization responses to histamine and pentagastrin actions on gastric gland cells to occur.

Key words: Hyperpolarization — Biphasic effect — Secretory cell — Secretion — Histamine — Pentagastrin

Introduction

It has been established that Ca ions play an important role in activation of secretory processes of many gland cells. The activation of salivary and gastric secretion by secretagogues seems to be dependent on the levels of extracellular calcium and these processes have been characterized by an enhanced calcium influx (Berglindth et al. 1980; Ginsborg and House 1980; Jiron et al. 1981; Soll 1981).

In absence of extracellular calcium ions when calcium stores in the gastric mucosa and the salivary glands become depleted, secretion mediated by secretagogues is abolished.

Many data have been accumulated concerning a considerable influence of extracellular calcium on electrical activity of salivary gland cells (Ginsborg et al. 1974; Ginsborg et al. 1980).

The present paper deals with the effect of extracellular calcium on the electrical activity of gastric gland cells induced by histamine and pentagastrin.

Fig. 1. Hyperpolarizing response of gastric gland cell to histamine (10^{-4} mol/l). *RP* — resting potential; *HR* — hyperpolarizing response.

Materials and Methods

Experiments were performed on isolated rat gastric mucosa. Membrane potentials were recorded from gastric gland cells using intracellular microelectrodes. Glass microelectrodes filled with 2.5 mol/l KCl and having a resistance of 25—30 MΩ were used.

Isolated rat gastric mucosa was placed into a chamber perfused with 36 °C warm normal Krebs solution of the following compositions (mmol/l): NaCl 135; KCl 4.7; $CaCl_2$ 2.5; $NaHCO_3$ 16.3; NaH_2PO_4 1.4; glucose 7.9.

To study the role of calcium in electrical responses of gastric gland cells to histamine, low-calcium (10^{-3} mol/l, 0.5×10^{-3} mol/l) and calcium-free solutions were used.

Following blockers of calcium currents were used: Co^{2+}, Cd^{2+}, Ni^{2+} (10^{-3} mol/l). The effect of blockers was studied in the Ringer-Locke solution to avoid Me^{2+} chelating properties of the Krebs solution.

Histamine (10^{-4} mol/l) and pentagastrin (6.5×10^{-9} mol/l) were used as the stimulators of gastric secretion. The cells were labelled by Li-carmin (Mitarai 1960; Villegas 1962) to enable the identification of gastric gland cells.

Results

The resting membrane potential (*MP*) of gastric gland cells (-24.2 ± 1.2 mV, $n = 147$) recorded in our experiments during 20—40 min showed no spontaneous fluctuations. In response to histamine (10^{-4} mol/l, Fig. 1) the membrane potential of some gastric gland cells was shifted to -44.5 ± 1.5 mV ($n = 51$).

Under the influence of pentagastrin the membrane potentials of gastric gland cells was shifted to -54.8 ± 1.4 mV ($n = 64$).

Hyperpolarization was the main response of gastric gland cells to secretagoues administered into Krebs and Ringer-Locke solutions; however, in a small proportion of cells (6—8 %) biphasic responses were recorded: an initial short-term depolarization followed by a prolonged and significant hyperpolarization (Fig. 2).

The hyperpolarizing responses to histamine were dependent on the calcium concentration in the bathing solution. In low-calcium solutions these responses significantly decreased while the resting membrane potentials of gastric gland cells remained unchanged.

In Krebs solutions containing 10^{-3} mol/l and 0.5×10^{-3} mol/l Ca ions hyper-

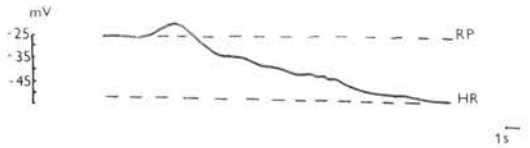

Fig. 2. Biphasic response of gastric gland cells to pentagastrin (6.5×10^{-9} mol/l).

polarization reached to -35.3 ± 1.3 mV ($n = 53$) and -28.5 ± 1.2 mV ($n = 47$), respectively.

Also, in low-calcium solutions the hyperpolarizing component of the biphasic response to histamine decreased. After a prolonged incubation (40 min) of the gastric mucosa in a calcium-free solution histamine did not induce any hyperpolarizing responses of gastric gland cells while the resting potential of the gastric gland cells remained unchanged. Effects of low-calcium and calcium-free solutions were reversible.

In the presence of Cd, Co and Ni ions (10^{-3} mol/l) the hyperpolarizing response of gastric gland cells to histamine decreased. It was shifted to -36.2 ± 0.7 ($n = 30$), 30.5 ± 0.84 ($n = 28$) and 38.3 ± 0.8 ($n = 32$), respectively. After the first 30 min responses of gastric gland cells to histamine were completely suppressed. In the presense of Co and Ni ions (10^{-3} mol/l) hyperpolarizing responses of gastric gland cells to pentagastrin were also decreased. The membrane potential of these cells reach -36.8 ± 1.0 mV ($n = 33$) and -39.2 ± 0.9 mV ($n = 35$), respectively. After 30 min no hyperpolarizing response to pentagastrin was observed. Solutions containing blockers of the calcium current had no effect on the resting potential of the gastric gland cells.

Discussion

In the present study two types of responses to histamine and pentagastrin have been observed. The first and dominant type has hyperpolarization, the other being biphasic response. Results obtained in the present study were in many respects similar to those reported for salivary gland cells and hepatocytes (Nishiyama 1973; Graf and Petersen 1978; Wakui and Nishiyama 1980).

The effects of histamine and pentagastrin on the electrical activity of gastric gland cells was dependent upon the concentration of extracellular calcium. Hyperpolarizing responses to these secretagogues were markedly diminished upon a reduction of the calcium concentration from 2.5 to 0.5×10^{-3} mol/l. The effect of the low calcium concentration was reversible. Studies with the calcium current blockers provided further evidence for a dependence of the effect of secretagogues

on extracellular calcium. The addition of blockers to the Krebs solution resulted in a marked supression of hyperpolarizing responses to histamine and pentagastrine. Calcium current blockers depressed calcium movement across the plasma membrane through calcium channels.

In several secretory cells, including gastric gland cells and salivary gland cells (Berlindth et al. 1980; Ginsborg and House 1980; Jiron et al. 1981), the activation of secretory processes by certain secretagogues the presence of extracellular calcium and was associated with an enhanced calcium influx upon activation. Thus we can assume that the hyperpolarizing responses to histamine and pentagastrin were also accompanied by an enhanced calcium influx. This in turn resulted in an increase in the permeability of gland cells for potassium (Ginsborg et al. 1974). The mechanism underlying hyperpolarization induced by histamine and pentagastrin may be an increase in the permeability of the membrane for potassium.

The ionic mechanism of the biphasic response of gastric gland cells is not clear. We suppose that these is no direct relationship between membrane hyperpolarization and secretion. Hyperpolarization could also be a secondary phenomenon only.

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