Electrical and mechanical interaction between circular and longitudinal muscle layers of the guinea-pig stomach

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Abstract

Sakamoto, Y. and Nasu, Y. Electrical and mechanical interaction between circular and longitudinal muscle layers of the guinea-pig stomach. Japanese Journal of Smooth Muscle Research, 23 (2), 67-73, 1978 — The effects of prostaglandin E1 and F2α on the mechanical and electrical responses of circular strips dissected from various parts of the guinea-pig stomach were examined. Prostaglandin E1 induced the tonic contraction without an inhibition of the phasic contraction in lower parts of stomach. The amplitude of tonic contraction decayed along with greater curvature of the stomach, that is, it was largest in pylorus region and smallest in upper corpus. Furthermore, the tonic contraction increased depending on concentrations of prostaglandin E1. When a longitudinal muscle layer was removed from the circular strips, the tonic contraction disappeared. On the other hand, prostaglandin E1 or F2α consistently induced an increase in the resting tone and the phasic contraction in longitudinal strips of all parts of stomach. Simultaneous recordings of the electrical and mechanical activities showed a correlation between membrane depolarization and tonic contraction induced by prostaglandin E1. Above results were not affected by nerve-blocking agent, atropine or tetrodotoxin. Thus it is suggested that the tonic contraction in circular strips induced by prostaglandin E1 is closely related to the longitudinal tonic contractions.

Introduction

In the isolated circular strips separated from longitudinal layers, taken from pylorus and antrum of guinea-pig stomach, spontaneous phasic contractions were inhibited by prostaglandin E2 (PGE2; Mishima and Kuriyama, 1976; Nitta and Ishizawa, 1980). In intact circular strips taken from fundus and corpus of the same organ, high concentrations of PGE1 (1.4×10⁻⁶ M) or PGE2 (1.4×10⁻⁶ M) induced a biphasic effect consisting of an initial, slight stimulation of the tone followed by an inhibition of it (Milenove et al., 1980). Furthermore, it is recently reported that electrical activities of cat intestine (Suzuki et al., 1986) and dog intestine (Hara et al., 1986), and mechanical responses to acetylcholine (Ach) are different on various parts of guinea-pig stomach (Komori and Suzuki, 1986). In intestinal smooth muscle of canine, mechanical responses to Ach and high K were different depending on muscle layers (Hara and...
Szurszewski, 1986). It is evident that effects of prostaglandin E₁ on the guinea-pig stomach muscle are quite different depending on regions and are entirely different on experimental conditions whether the one muscle preparation contains the other muscle layer or not. Therefore, the aim of the present study was to clarify the reason why there was such a difference between the intact and isolated circular muscles of the guinea-pig stomach.

**Methods**

Guinea-pig of either sex and of 250-300 g body weight were killed by cervical dislocation. The stomach was excised and strips of circular muscles attached with longitudinal muscle layers (1 mm width, 5 mm length) were dissected from various parts of stomach (Fig. 1). In most of experiments, the intact circular strips attached with longitudinal muscle layers were used. In some experiments, however, isolated circular strips, which were mechanically separated from the longitudinal muscle layer, were used. Under a stereo-microscope the mucous membrane was removed from these strips. The preparation was suspended in a 1 ml organ bath which was superfused by krebs solution maintained at 36°C and gassed with 3% CO₂ in oxygen. The circular contractions were recorded isometrically with a force displacement transducer (Shinkoseiki-U2) linked to a potentiometric pen-recorder (Nihon koden, RJG-4022). The resting tension was adjusted to 0.2 g and the preparation allowed to equilibrate for 120 min to obtain constant contraction before start of the experiments. The Krebs solution used in all experiments had the following composition (mM): NaCl 120, KCl 5.9, CaCl₂ 2.5, NaHPO₄ 1.2, MgCl₂ 1.2, NaHCO₃ 15.5, and glucose 11.5.

Drugs used, freshly dissolved in a distilled water to make up stock solutions, were; prostaglandins (PGE₁ and PGF₂α) (Ono pharm. Co. Ltd.), atropine sulphate (Merk) and tetrodotoxin (TTX, Sankyo). The drugs were added to reservoir to be required concentrations. To obtain simultaneous recordings of electrical and mechanical activities in the muscle cells, double sucrose-gap method was used. In other experiments, conventional microelectrode technique was used to confirm the electrical results obtained by sucrose-gap method.

![Fig. 1. Schematic diagram of the guinea-pig stomach and the localization of the smooth muscle strips. The preparation designated as alphabets: p, l, m, u and f were dissected from the pyloric antrum, lower-, middle- and upper-corpus and fundus in circular direction, respectively and L was dissected in the longitudinal direction in the lower corpus region.](image)
Results

1. Tonic contraction-relaxation profile to PGE₁

When prostaglandin E₁ F₂α (PGE₁: 10⁻⁷ g/ml) or prostaglandin F₂α (PGF₂α: 10⁻⁷ g/ml) was applied to various preparations taken from as shown in Fig. 1 in the Krebs solution, combined phasic-tonic contraction and inhibition were observed as shown in Fig. 2. The tonic contractions were conspicuous in the pyloric antrum (Fig. 2Ap) and such contraction gradually decayed along with ascending portions of stomach, and in upper corpus tonic relaxation was marked (Fig. 2Au). The amplitude of the phasic contraction was reduced by PGE₁ in upper corpus, but increased in lower corpus (Fig. 2Ap and u). In contrast to PGE₁, PGF₂α induced only contractile responses in all parts of the stomach, and the amplitude of tonic contraction was greater in upper corpus than in pyloric antrum (Fig. 2B). The tonic contraction-relaxation profile induced by PGE₁ were not significantly affected by atropine (10⁻⁶ M) or tetrodotoxin (10⁻⁷ M) in all parts of stomach (Fig. 3 and 4). Furthermore, the amplitude of tonic contraction in the lower corpus region increased in concentrations-dependent manner as shown in Fig. 4. Similar results were also obtained in all other parts of stomach (not shown here).

On the other hand, only tonic and phasic contractions were observed in longitudinally dissected preparations from all parts of stomach in the presence of PGE₁ or PGF₂α (not shown here).

2. Relaxation to PGE₁

As shown in the left panel of bottom records of Fig. 5, tonic response to PGE₁ (10⁻⁷ g/ml) was disappeared in an isolated circular muscle strips of lower corpus. The disappearance of the tonic contraction was not observed even in high concentrations of PGE₁ (10⁻⁶ g/ml). In

Fig. 2. Effects of PGE₁ (10⁻⁷ g/ml) and PGF₂α (10⁻⁷ g/ml) on the circular preparations. Column A shows various responses to PGE₁ and column B to PGF₂α in each circular preparation as shown by alphabets in Fig. 1. Note a decay of the tonic contraction along with ascending portion of stomach. All contractile responses to PGE₁ and PGF₂α were obtained from the same stomach.
contrast to the intact circular muscle, the isolated circular muscle did not show any tonic contraction at all even in high concentrations of PGE₁ (10⁻⁵ g/ml). However, any difference of contractile responses to acetylcholine (10⁻⁷ M) between the isolated and intact circular strips was not observed (Fig. 5, right panels). The tonic inhibition, as observed in the isolated muscles, marked in upper corpus region.

3. Electrical responses to PGE₁

Simultaneous recordings of the electrical and mechanical activities in the intact circular muscle strips were obtained by double sucrose-gap method as shown in Fig. 6A. An increased resting tone corresponding to a slight depolarization was obtained in the presence of PGE₁ (10⁻⁷ g/ml). The amplitude of phasic contraction and duration of second component in the slow wave (see Ohoba et al., 1975) were reduced by PGE₁. The effect of the drug on the electrical activity was confirmed by intracellular recording, that is, the duration of the second component in the slow wave was also reduced in the intact- and isolated- circular preparations (Fig. 6B
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A Cir. with long.  
PGE$_1$, 10$^{-7}$ g/ml

B Cir. without long.  
ach, 10$^{-7}$ g/ml

Fig. 5. Effects of mechanical removal of longitudinal layers on the PGE$_1$ (10$^{-7}$ g/ml)-induced tonic contraction. Records in the intact circular preparations (A) show control responses to PGE$_1$ and Ach. Records in the isolated circular preparations (B) (without longitudinal muscle layers) show a disappearance of contractile responses to PGE$_1$ but a contractile responses to Ach. Maximum deflexion of records in right hand during Ach was cut.

and C). Furthermore, the membrane was slightly depolarized (2-3 mV) by PGE$_1$ in the intact circular preparations (Fig. 6B), but slightly hyperpolarized (2-3 mV) in the isolated one (Fig. 6C). The reduction in the duration of the slow wave has been also observed in canine antral circular muscle (Sanders, 1984). These effects of PGE$_1$ on the electrical and mechanical events were not also modulated by atropine (10$^{-6}$ M) and TTX (10$^{-7}$ M).

Discussion

Tonic contraction-relaxation profile in the circularly dissected preparations of the guinea-pig stomach was observed.

The tonic contraction is conspicuous in the preparation taken from pyloric antrum. On the contrary, the tonic relaxation was conspicuous in upper corpus region. These contraction and relaxation were not influenced by atropine and TTX (Fig. 3 and 4), thus tonic contraction-relaxation profile induced by PGE$_1$ is due to muscular origin rather than nervous system.

Further, the tonic contraction disappeared in the circularly dissected strips from which longitudinal layer was removed. The disappearance of tonic contraction is not due to a mechanical damage, since the response to acetylcholine is not affected by mechanical removal of muscle layer (Fig. 5). If the tonic contraction induced by PGE$_1$ is originally initiated in the circular muscle itself, it should be induced in the isolated circular muscle. However, the tonic contraction was not observed in the isolated circular muscle.

Simultaneous recordings of the electrical and mechanical responses to PGE$_1$ show the correlation between a slight depolarization and tonic contraction in the intact circular strips. This depolarization was confirmed by using intracellular recordings in the intact circular muscle, but in the isolated circular muscles, the membrane was inversely hyperpolarized by
Fig. 6. Effects of PGE$_1$ (10$^{-7}$ g/ml) on the electrical and mechanical activities of the circular muscles. Records (A) were obtained by the sucrose-gap method. Upper and lower traces in (A) were continuous recording of the mechanical and electrical activities, respectively. Note the simultaneous depolarization and an increase in resting tone during PGE$_1$. Broken lines showed levels in the resting potential and tone. Records (B) and (C) were obtained from the intact-and isolated circular muscle strips, respectively, by using conventional microelectrode technique. Upper and lower in each record show the continuous recordings of the electrical activities. Horizontal lines in the all traces indicated the application time of the drug. Time scale in the left hand was different from that in the right.

PGE$_1$. Similar hyperpolarization of the circular muscle membrane has been reported in the same muscles by Mishima and Kuriyama (1976). Further, they also showed the membrane depolarization induced by PGE$_1$ in the longitudinal muscle of the stomach. It has been shown that an electrical coupling between the longitudinal- and circular-muscle layers has existed in the cat’s intestine (Connor et al., 1977; Taylor et al., 1977). In addition, electron microscopic observations reveal an abundance of interstitial cells and fibrocytes in the region between the muscle layers which make junctional contacts with muscle fibers of each layer and with each others in the cat’s small intestine (Taylor et al., 1977). Further, mechanical interaction between longitudinal and circular axes of the small intestine in the same animal has been reported by Wood and Perkins (1970). In the stomach muscles, the amplitude of tonic contraction was greatest in the pyloric antrum and yet decreased along with the ascending portion of stomach. Further, the depolarization and the tonic contraction of circular muscle were not observed in the isolated circular muscle. Based on above evidences and present results, it would be hypothetically proposed that the depolarization of longitudinal muscle electrotonically spreads to the circular muscle through some pathway. This pathway may be interstitial cells rather than nervous system, since the tonic contraction-relaxation profile were not
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Recently, it has been reported that the interstitial cells of Cajal are different from a gap junction, but they are supposed to be pathway of electrical activities (Suzuki et al., 1986). These proposal also support previous hypotheses. From above hypotheses, question, why the depolarization of the longitudinal muscle by PGE1 does not trigger extra spike activities on the slow waves of the circular muscle, is immediately raised. However, it may be neglected, since the isolated circular muscle membrane is slightly hyperpolarized by PGE1. Thus, the hyperpolarization of the circular muscle membrane may fail to trigger extra activities by reducing depolarizing signal from the longitudinal muscle layers. However, in the intact circular preparations, depolarizing signal from the longitudinal muscle may spread to the circular muscle layer resulting in slight depolarization, but the depolarization may not be enough to trigger spike activities in the circular muscles.

References