PO Box 2345, Beijing 100023, China
Fax: +86-10-85381893
E-mail: wjg@wjgnet.com www.wjgnet.com

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Effect of cholecystokinin and secretin on contractile activity of isolated gastric muscle strips in guinea pigs

Li W, Zheng TZ and **Qu SY**

Subject headings gastric muscle strips; cholecystokinin; secretin; guinea pigs

Abstract

AIM To study the effect of cholecystokinin-octapeptide (CCK- 8) and secretin on contractile activity of isolated gastric muscle strips in guinea pigs.

METHODS Each isolated gastric muscle strip was suspended in a t issue chamber containing 5 mL Krebs solution constantly warmed by water jacked at 37 ℃ and supplied with a mixed gas of 95% O_2 and 5% CO_2. After incubating for 1h under 1g tension, varied concentrations of CCK-8 and se cretin were added respectively in the tissue chamber and the contractile response was measured isometrically on ink-writing recorders.

RESULTS CCK-8 could increase ① all regional circular and longitudinal muscular tension at rest (fundus LM 19.7%±2.1%, *P*<0.01; fundus CM 16.7%±2.2%, *P*<0.01; gastric body LM 16 .8% ±2.3%, *P*<0.01; body CM 12.7%±2.6%, *P*<0.01; antrum LM 12.3%±1.3%, *P*<0.01; antrum CM 16.7%±4.5%, *P*<0.01; pylous CM 12.7%±5.0%, *P*<0.05); ② contractile frequencies of body LM, both LM and CM of antrum and pylorus CM (5.1/min±0.2/min to 5.6 /min±0.2/min, 5.9/min±0.2/min to 6.6/min ±0.1/min, 5.4/min±0.3/min to 6.3/min±0.4/ min, 1.3/min±0.2/min to 2.3/min±0.3/min, respectively, *P*<0.05); ③ the mean contractile amplitude of antral circular mus cle (58.6%± 18.4%, *P*<0.05) and ④ the motility index of pylorus CM (145.0%±23.8%, *P*<0.01), but decrease the mean contractile ampl itude of gastric body and antral LM (-10.3%±3.3%, -10.5%±4.6%, respectively, *P*<0.05). All the CCK-8 effects were not blocked by atropine or ind omethacin. Secretin had no effect on gastric smooth muscle activity.

CONCLUSION CCK-8 possessed both excitatory and inhibitory action on contractile activity of different regions of stomach in guinea pigs.Its action was not mediated via cholinergic M receptor and endogenous prostaglandin receptor.

Wei Li, Tian Zhen Zheng and Song Yi Qu
Department of Physiology, Lanzhou Medical College, Lanzhou 730000, Gansu Province, China
Wei Li, female, born on 1952-06-07 in Taiyuan, Shanxi Province, graduated from Lanzhou Medical College in 1977, now associate Professor of physiology, majoring digestive physiology, having 25 papers published.
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Correspondence to: Wei Li, Department of Physiology, Lanzhou Med ical College, Lanzhou 730000, Gansu Province, China.
Tel. +86-931-8289531
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INTRODUCTION

CCK and secretin have important actions on gastrointestinal motility *in vivo* and *in vitro*, but few reports have covered the gastric smooth muscle motili ty in guinea pigs. In this paper, we studied the action of CCK and secretin on isolated gastric smooth muscle in guinea pigs and compared it with those of the corresponding regions in rats[1].

MATERIAL AND METHODS

Guinea pigs, weighing 250 g-350 g, male or female, were fasted but with free access to water for 24 h, hit the head to lose consciousness and the whole stomach was removed. The stomach was opened along the greater curvature and muscle strips (8 mm×2 mm) were cut, parallel to either the longitudinal or circular fibers [longitudinal muscle (LM) and circular muscle (CM) of fundus, body, antrum and CM of pylorus]. After remoral of mucosa, each strip was suspended in tissue chamber containing 5 mL Krebs solution and constantly warmed by circulating water jacked at 37 ℃ and supplied with 95% O_2 and 5% CO_2. One end of the strip was fixed to hook on the bottom of the chamber while the other one was connected by thread to an external isometric force transducer (JZ-BK, BK) at the top. Preparations were subjected to 1 g load tension and washed with 5 mL Krebs solution every 20 min. The contractions of gastric strips in 7 tissue chamber were simultane ously recorded on ink-writing recorders (LMS-ZB, Chengdu)[2]. After incubating for 1 h, CCK-8 (10^{-1} μmol/L, 10^{-2} μmol/L, 5×10^{-2} μmol/L) or secretin (10^{-1} μmol/L, 10^{-2} μmol/L, 5×

10^{-2} μmol/L) was added to the tissue chamber separately. CCK-8 and secretin were added together at the same time. To attain the final concentration 50 μL of reagent were added in a 5 mL bath.

We measured the resting tension of every strip, mean contractile amplitude of muscle strips of gastric body and antrum and the motility index [MI = ∑ (amplitude×duration) of CM strips of pylorus. Frequencies of contraction were calculated by counting the contraction waves per minute. The results were presented by the increased percentage (%) of spontaneous contraction ($\bar{x}\pm s_{\bar{x}}$ %). The data were analyzed by Student's *t* test, and *P* values <0.05 were considered as significant[3].

RESULTS

Effects of CCK-8 on spontaneous contraction of gastric muscle strips

CCK-8 increased the resting tension of muscle strips in various regions of the stomach (Table 1), the mean contractile amplitude of antral CM and the motility index of pyloric CM, but decreased the mean contractile amplitude of body and a ntrum LM (Table 2), which were concentration-dependent. It also increased contractile frequencies of body LM, both LM and CM of antrum and pylorus CM (5.1/min±0.2/min to 5.6/min±0.2/min, 5.9/min±0.2/min to 6.6/min±0.1/min, 5.4/min±0.3/min to 6.3/min±0.4/min, 1.3/min±0.2/min to 2.3/min±0.3/min, respectively, *P*<0.05).

Atropine (10^{-2} mmol/L) decreased the tension of gastric muscle strips the mean contractile amplitude and the motility index of gastric strips in varyin g degrees but did not significantly affect the frequency of contractions. Atropi ne (10^{-2} mmol/L) given 3 min before administration of CCK-8 (10^{-2} μmol/L) did not affect the CCK-8 action on gastric strips (Tables 1, 2).

Table 1 Effects of CCK-8 on the resting tension of gastric strips in guinea pigs

Part of stomach		CCK-8	CCK-8+secretin	Atropine and CCK-8		Indomethacin and CCK-8	
Fundus	LM	19.7±2.1[b] (*n* = 19)	23.1±2.1[b] (*n* = 17)	-25.1±4.0[b] (*n* = 17)	47.1±6.0[b] (*n* = 17)	-34.5±4.4[b] (*n* = 17)	37.6±5.6[b] (*n* = 17)
	CM	16.7±2.2[b] (*n* = 16)	16.0±1.8[b] (*n* = 15)	-14.9±2.5[b] (*n* = 17)	35.2±6.5[b] (*n* = 17)	-14.1±3.2[b] (*n* = 17)	30.3±7.0[b] (*n* = 17)
Body	LM	16.8±2.3[b] (*n* = 19)	20.4±1.9[b] (*n* = 17)	-21.7±3.4[b] (*n* = 17)	18.3±2.8[b] (*n* = 17)	-8.3±3.1[a] (*n* = 16)	13.0±1.7[b] (*n* = 16)
	CM	12.7±2.6[b] (*n* = 11)	15.9±3.3[b] (*n* = 13)	-6.7±1.8[b] (*n* = 15)	18.3±2.4[b] (*n* = 15)	-5.7±1.8[a] (*n* = 14)	12.3±2.1[b] (*n* = 14)
Antrum	LM	12.3±1.3[b] (*n* = 13)	11.6±2.0[b] (*n* = 15)	-2.9±1.2[a] (*n* = 14)	8.6±1.7[b] (*n* = 14)	-1.9±0.8[a] (*n* = 14)	4.9±0.9[b] (*n* = 14)
	CM	16.7±4.5[b] (*n* = 11)	28.4±4.1[b] (*n* = 17)	0 (*n* = 14)	23.8±4.1[b] (*n* = 14)	5.0±5.0 (*n* = 16)	30.0±4.8[b] (*n* = 16)
Pylorus	CM	12.7±5.0[a] (*n* = 10)	8.9±3.1[a] (*n* = 12)	0 (*n* = 13)	8.2±2.4[a] (*n* = 13)	0 (*n* = 10)	8.0±3.4[a] (*n* = 10)

L(C)M, longitudinal (circular) muscle; dose: CCK-8 10^{-2}μmol/L, secretin 10^{-2}μmol/L; atropine 10^{-2}mmol/L, indomethacin 10^{-2}mmol/L; [a]*P*<0.05, [b]*P*<0.01 *vs* control; 0, no effect; $\bar{x}\pm s_{\bar{x}}$% increase.

Table 2 Effects of CCK-8 on the mean contractile amplitude of body and antrum, and the motility index of pylorus in guinea pigs

Part of stomach		CCK-8	CCK-8+secretin	Atropine and CCK-8		Indomethacin and CCK-8	
Body	LM	-10.3±3.3[a] (*n* = 19)	-8.4±3.4[a] (*n* = 17)	-17.1±4.8[b] (*n* = 17)	1.5±2.1 (*n*=17)	-8.6±2.7[a] (*n*=16)	-9.7±3.3[a] (*n* = 16)
	CM	-2.3±2.3 (*n* = 11)	0 (*n* = 13)	-23.3±6.6[b] (*n* = 15)	0 (*n* = 15)	0 (*n* = 14)	0 (*n* = 14)
Antrum	LM	-10.5±4.6[a] (*n* = 13)	-9.9±4.3[a] (*n* = 15)	-22.2±5.9[b] (*n* = 14)	-12.3±4.8[a] (*n* = 14)	-8.2±2.6[a] (*n* = 14)	-10.0±2.9[a] (*n* = 14)
	CM	58.6±18.1[a] (*n* = 11)	48.8±10.8[b] (*n* = 17)	-15.7±5.4[a] (*n* = 14)	49.8±11.6[b] (*n* = 14)	0 (*n* = 16)	45.6±6.6[b] (*n* = 16)
Pylorus	CM	145.0±23.8[a] (*n* = 10)	162.5±31.7[a] (*n* = 12)	-41.9±12.2[a] (*n* = 13)	161.5±55.0[a] (*n* = 13)	0 (*n* = 10)	140.0±21.9[b] (*n* = 10)

L(C)M, longitudinal (circular) muscle; dose: CCK-8 10^{-2}μmol/L, secretin 10^{-2}μmol/L; atropine 10^{-2}mmol/L, indomethacin 10^{-2}mmol/L; [a]*P*<0.05, [b]*P*<0.01 *vs* control; 0, no effect; $\bar{x}\pm s_{\bar{x}}$% increase.

Indomethacin (10^{-2} mmol/L) also decreased the resting tension and the mea n contractile amplitude, but did not significantly affect the frequency of contractions. Indomethacin (10^{-2} mmol/L) given 3 min before administration of CCK-8 (10^{-2} μmol/L) similarly did not affect the CCK-8 action on gastric strips (Tables 1, 2).

Effects of secretin on the spontaneous contraction of gastric strips

Secreatin (10^{-1} μmol/L, 10^{-2} μmol/L, 5×10^{-2} μmol/L) did not significantly affect the resting tension, the mean contractile amplitude, the motility index and the contractile frequency on gastric strips.

Effects of combined CCK-8 and secretin on the spontaneous contraction of gastric strips

When CCK-8 (10^{-2} μmol/L) and secretin (10^{-2} μmol/L) were combined, the effect was similar to CCK-8 (10^{-2} μmol/L) alone (Tables 1, 2).

DISCUSSION

CCK-8 could increase the mean contractile amplitude of antral CM and motility i ndex of pyloric CM of guinea pigs which was similar to that seen in rats[1]. CCK-8 increased the resting muscle tension, the contractile frequency of body LM, antral LM and CM and pyloric CM, it decreased the mean contractile ampl itude of body and antral LM, but did not affect the gastric strips of the corre sponding regions in rats. Meanwhile, the mechanism of action of CCK-8 on gastric smooth muscle has not been elucidated. Grider *et al*[4] considered CCK-8 could contract isolated CM of body in guinea pigs, but it was not blocked by TTX and atropine, therefore CCK-8 might have direct effect on smooth muscle cell. Gerner[5] believed that CCK-8 could increase the resting tension of fundus, and contractile amplitude of antrum which could be partly mediated via cholinergic nerve pathway. Our results demonstrated that the CCK-8 effect was neither blocked by atropine nor blocked by indomethacin, it suggests that action of CCK-8 is not mediated via prostaglandin. The fact that CCK-8 increased the contractile frequency of gastric strips in guinea pigs as well as in dogs required further study[6]. Secretin did not affect gastric strips activity obviously in guinea pigs and when CCK-8 and secretin were combined the effect was similar to that of CCK-8 alone. It showed that secretin neither affect t he isolated gastric strips in guinea pigs nor affect the action of CCK-8 on gastric strips, but secretin decreased the resting tension of LM and CM of fundus, and body, the mean contractile amplitude of LM and CM of antrum in rats. When CCK-8 and secretin were combined, the action the increase in mean contractile am plitude of LM and CM of antrum by CCK-8 was eliminated in rats. There was m arked discrepancy in response to secretin in isolated gastric strips of guinea pigs and rats. It was reported that guinea pig had a special gastrointestinal pancreas system[7], whether these are related to the above factor as yet could not be answered. CCK-8 and secretin both have physiological modulating function on gastric emptying in rats[8], whether the same occurs in the guinea pigs, need further studies.

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