EFFECT OF CHOLECYSTOKININ OCTAPEPTIDE ON CONTRACTION OF BOVINE RUMINAL MUSCLE

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Introduction

Various studies have been made recently to clarify the role of cholecystokinin octapeptide (CCK-8) in gastrointestinal motility in many species (Milenov, 1987; Raybould, 1987; Wiley, 1987). The inhibitory effect of CCK-8 has been reported on reticular and abomasal motility in cattle (Ruckebusch, 1983) and on ruminal motility in sheep (Onodera, 1989) in vivo. However, the direct effect of CCK-8 on the ruminal muscle in vitro has not been reported. The present study was done to investigate whether CCK-8 acts directly on isolated bovine ruminal muscle and whether CCK-8 interacts with acetylcholine (Ach) in this preparation.

Materials and Methods

The segmental walls of the cranial sac of the rumen were dissected from 12 heads of cattle freshly slaughtered at the local abattoir. After removal of the mucosa and serosa, muscle strips 20 mm long and 1-2mm wide, were obtained from the circular muscle layer and the longitudinal muscle layer. These strips were investigated in thermostatically controlled (37°C) organ baths (25 ml) filled with Krebs-Henseleit solution. The preparations were allowed to equilibrate for 60-90 min in the bath, and the solution was changed at 30 min intervals. CCK 8 or Ach was added to the bath in increasing concentrations to determine the concentration response. The final CCK-8 concentrations in the bath ranged from $1x10^{-13}$ to $1x10^{-7}$ M and Ach concentrations ranged from $1x10^{-6}$ to $2x10^{-4}$ M. A further experiment was carried out to elucidate the interaction between Ach and CCK-8. Ach was added independently to the bath in a $5x10^{-5}$ M (ED_{50}) final concentration and the response was recorded for 3 min. After the solution in the bath was washed out three times and the muscle strip was equilibrated for 11 min, Ach and CCK-8 were added simultaneously to the bath, resulting in $5x10^{-5}$ M and $1x10^{-9}$ M final concentrations, respectively. Isometric contractions were recorded with a force-transducer, an amplifier and a pen-recorder. The student's t-test was used for making statistical analysis and a P value of 0.05 or less was considered statistically significant.

Results

Strips from both the circular muscle (Ci) and the longitudinal muscle (Lo) responded dose-dependently with a mono-phasic contraction to

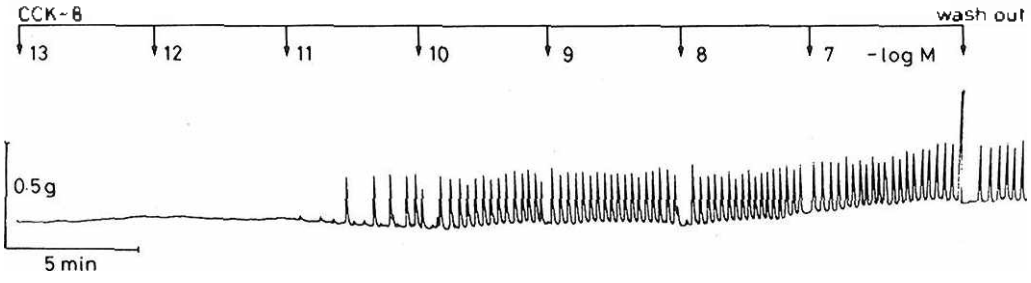

Figure 1. Effect of CCK-8 on circular muscle obtained from the cranial sac of the bovine rumen. Arrows indicate the addition of CCK-8 to the bath medium in increasing concentrations. Vertical lines represent the scale of isometric tension.

Ach. The maximal contraction was observed in the $1x10^{-2}$ M concentration, and the ED_{50} was $5x10^{-5}$ M in both the Ci and the Lo strips. CCK-8 induced phasic contractions in the strips without spontaneous phasic contractions and the frequency was increased in a dose-dependent manner in both types of muscle strips (figure 1). The maximal amplitude of phasic contractions was 23.0% of the response to Ach ED_{50} in Ci and 2.8% in Lo. CCK-8 also produced tonic contraction in both types of muscle. The maximal amplitude was attained at 10^{-8} M in Ci and 10^{-7} M in Lo, indicating 24.2% and 6.5% of the response to Ach ED_{50}, respectively. CCK-8 ($1x10^{-9}$ M) added with Ach ED_{50} ($5x10^{-5}$ M) did not inhibit the response of either the Ci or the Lo strips to Ach ED_{50} added by itself. Conversely, the contraction amplitude of the Ci was increased by 18.4%, though this increase was not significant.

Discussion

CCK-8 induced tonic and phasic contractions in isolated preparations of ruminal smooth muscle and did not inhibit the contractile response to Ach in these preparations. These results are incompatible with those reported that in vivo studies intravenous administration of CCK-8 inhibited the ruminal motility (Onodera, 1989). This inconsistency indicates that the inhibition of ruminal motility resulted from CCK-8 action other than direct CCK-8 effects on the ruminal muscle, though further studies are necessary to clarify whether CCK-8 in the present study acted directly on ruminal muscle or acted indirectly, mediating the Auerbach's plexus. Rumen contractions are caused by nervous activity emanating from gastric centres through vagal nerve fibres. CCK-8 might inhibit the activity of gastric centres though the site of the CCK-8 inhibitory action has not been clarified.

(Key Words: CCK-8, Bovine Ruminal Muscle, Contraction)

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