Effects of Prostaglandins $E_2$ and $F_{2\alpha}$ on Electromyogram of Cat Colon in Vitro

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Prostaglandins cause diarrhea, and their production by the gut increases in diarrheal states. We studied the effects of PGF$_{2\alpha}$ and PGE$_2$ on the electromyogram recorded from the cat colon in vitro to determine if these prostaglandins might produce electromyographic changes similar to those seen in diarrheal states. PGF$_{2\alpha}$ decreased slow wave frequency and uncoupled slow wave propagation in the proximal colon. It increased the frequency of migrating spike bursts. PGE$_2$ had no effect on slow waves, but increased the frequency of the migrating spike burst. PGF$_{2\alpha}$ produced electromyographic changes similar to those recorded from the colon of cats with spontaneous diarrhea or after exposure to diarrhea-producing agents such as ricinoleate or quinidine. Some diarrhea-producing agents are likely to act by increasing prostaglandin production.

KEY WORDS: slow waves; colonic motility; colon; large intestine; gastrointestinal motility.
PROSTAGLANDINS AND CAT COLON

The normal myoelectrical activity of the colon is disrupted in cats with epidemic diarrhea or diarrhea produced by agents such as castor oil, ricinoleate (the active agent in castor oil), or capsaicin (19-22). Under these conditions the normal pacemaking mechanism of the colon is replaced by many pacemakers in the ascending colon operating independently at different frequencies.

The purpose of these studies was to determine the effects of PGE2 and PGF2α on electromyograms recorded from cat colon in vitro.

MATERIALS AND METHODS

Adult cats of both sexes weighing at least 2.0 kg were anesthetized with sodium pentobarbital (50 mg/kg). The colon was measured in situ. The ileum was transected 1 cm above the ileocecal junction, and the colon was transected where the colon entered the pelvis. The abdominal colon was removed, opened longitudinally along its antimesenteric border and cleaned with Krebs solution. The tissue was pinned mucosal surface up in a bath of Krebs solution equilibrated with 95% O2-5% CO2 and warmed to 37°C. The mucosa was removed by sharp dissection, and a strip of colonic muscle measuring 1 cm by the entire length of colon was cut in the longitudinal axis along the mesenteric border and cleaned with Krebs solution. The tissue was then exposed to either PGF2α (100 nM/ml) or PGE2 (10 nM/ml). During any experiment only one PG concentration could be used because tachyphylaxis occurred, an effect that was not reversed with up to a 3-hr washout. Prostaglandins were dissolved in ethanol but at its final bathing concentrations it had no effect on slow wave frequency at any concentration tested.

Electrode number 1 was located 1 cm distal to the ileocecal valve. Monopolar electrical recordings were made between these electrodes, and a common reference electrode was placed at one end of the bath. Records were made using the R-C input of a Beckman RM type Dynograph strip chart recorder with a time constant of 1 sec and a high-frequency filter diminishing electrical transients greater than 30 cps.

A baseline recording was made for the first 90 min of the experiment. The tissue was then exposed to either PGF2α, 1 ng/ml-1 μg/ml or PGE2, 10 ng/ml-1 μg/ml. During any experiment only one PG concentration could be used because tachyphylaxis occurred, an effect that was not reversed with up to a 3-hr washout. Prostaglandins were dissolved in ethanol but at its final bathing concentrations it had no effect on the electromyogram when tested alone.

Records were analyzed visually for slow wave and migrating spike burst frequencies for the last 15 minutes of the control, treatment, and recovery periods. Recordings from the proximal, middle, and distal pairs of electrodes were grouped for analysis of slow-wave frequency. Recordings from the mid-colon were analyzed for migrating spike burst frequency. Treatment groups were compared to controls by using a repeated measures analysis of variance and a confidence level of 1% was chosen. Results are expressed as mean ± SE.

RESULTS

Effects of Prostaglandin F2α on Electromyogram of Cat Colon. The basal slow wave frequency was 5.9 ± 0.2 cycles per minute (cpm) in the proximal colon, 6.0 ± 0.1 cpm in the mid-colon, and 6.0 ± 0.1 cpm in the distal colon. Low concentrations of PGF2α, (1 ng/ml and 10 ng/ml) decreased slow wave frequency slightly (P < 0.01) (Figures 1 and 2). Major changes of slow wave frequency and uncoupling of slow waves were seen when the tissue was exposed to 100 ng/ml PGF2α (Figures 1 and 2). Slow wave frequency in the proximal colon decreased to 2.7 ± 0.3 cpm, 4.7 ± 0.4 cpm in the mid-colon, and increased to 6.3 ± 0.2 cpm in the distal colon. The changes in slow wave frequency seen in the proximal and distal colon were statistically different from control values (P < 0.01). PGF2α concentrations at or above 100 ng/ml induced uncoupling of slow wave activity, lowering regional slow wave pacemakers to oscillate at their intrinsic frequencies. The maximal effect of PGF2α on slow wave frequency was seen at 100 ng/ml. At each PG concentration tested, slow wave frequency returned to control values after a 2-hr washout period. Even though slow wave frequency returned to normal values, the tissue exhibited refractoriness to further prostaglandin exposures.

There was a concentration-related, graded response of migrating spike burst frequency to PGF2α (Figure 3). The control migrating spike burst frequency was 0.33 ± 0.03 cpm. The lowest concentration of PGF2α tested, 1 ng/ml, increased the migrating spike burst frequency to 0.52 ± 0.03 cpm (P < 0.01). The maximal effect of PGF2α was seen at 100 ng/ml. This concentration produced a migrating spike burst frequency of 0.68 ± 0.08 cpm (P < 0.01). A 2-hr washout period returned migrating spike burst frequency to control values. In one experiment 100 ng/ml PGF2α produced continuous spiking activity. Changes in the electromyogram induced by PGF2α were apparent within 2 min of exposure.

Effects of PGE2 on Cat Colon. Prostaglandin E2 had no effect on slow wave frequency at any concentration tested (Figure 4). There was a concentration-related, graded effect of PGE2 on migrating spike burst frequency (Figures 4 and 5). The control migrating spike burst frequency was 0.29 ± 0.04 cpm. This was increased to a maximal frequency of 0.66 ± 0.09 cpm by 1 μg/ml PGE2 (P < 0.01). A 2-hr washout period returned migrating spike burst frequency to control values.

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