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The effect of intravenous prostaglandin $F_{2\alpha}$ and E_2 on the motility of the sigmoid colon

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SUMMARY The effect of a 20-min intravenous infusion of prostaglandin E_2 (0·08 μg kg^{-1} min^{-1}) or of prostaglandin $F_{2\alpha}$ (0·8 μg kg^{-1} min^{-1}) on the segmental pressures in the sigmoid colon was studied in 12 patients. Prostaglandin $F_{2\alpha}$ had no measurable effect, but prostaglandin E_2 significantly inhibited sigmoid motility.

The diarrhoea caused by prostaglandins (PGs) is one of the factors that limits the usefulness of these compounds in obstetrics. Prostaglandins may be the cause of diarrhoea associated with certain tumours and it has been suggested that they may play a part in the causation of some infective diarrhoeas (Williams, Karim, and Sandler, 1968; Sandler, Karim, and Williams, 1968; Pierce, Carpenter, Elliott, and Greenough, 1971). Absorption of water and electrolytes by the colon and the rate of transit of colonic contents are important determinants of the severity of faecal fluid loss in various diarrhoeal states (Cummings, James, and Wiggins, 1973; Waller, 1973). Colonic segmentation is thought to be one of the factors controlling the rate of colonic transit and low levels of segmental contraction are associated with diarrhoea (Waller, Misiewicz, and Kiley, 1972). We have studied the effect of intravenous $PGF_{2\alpha}$ and PGE_2 on segmental pressures in the sigmoid colon.

Methods and Patients

Intraluminal pressures in the sigmoid colon were measured with small (10 × 4 mm) rubber air-filled balloons attached to polyethylene tubes. The tube assembly was introduced through a sigmoidoscope and placed so that the recording balloon lay 20 to 25 cm proximal to the anal margin: the sigmoidoscope was then withdrawn, leaving the tube *in situ*. Pressures were recorded on a multichannel pen-writer (Sanborn) and the records were analysed by measuring the amplitude and duration of each pressure wave. Respiratory and somatic artefacts were monitored by a stethograph placed on the thorax. The results were expressed as mean amplitudes in cm H_2O of the pressure peaks and percentage duration of motor activity in each 10-min observation period, as defined previously (Misiewicz, Connell, and Pontes, 1966). Prostaglandins or 0·15 M NaCl were infused intravenously at a constant rate from motor-driven syringes.

The studies were performed on patients who had fasted overnight and who were not taking any drugs. Following intubation the patients reclined comfortably on a couch and 30 min were allowed to elapse before measurements were started. Colonic motility was recorded throughout the study. Intravenous saline was given for the first 30 min, followed by $PGF_{2\alpha}$ (0·8 μg kg^{-1} min^{-1}) or PGE_2 (0·08 μg kg^{-1} min^{-1}) for 20 min and then by saline for 30 min. For analysis of the results, the average values of mean amplitude and percentage duration of activity were calculated for the basal 30 min, the PG period, and the post-PG 30 minutes. Wilcoxon's paired rank sum test was used for calculation of statistical significance.

Twelve male patients were studied, all of whom gave their informed consent to the study. They all complained of abdominal pain, for which no cause was apparent on routine investigation: all had normal barium enema and sigmoidoscopic appearances.

Results

Intravenous infusion of $PGF_{2\alpha}$ at 0·8 μg kg^{-1} min^{-1} for 20 min did not affect colonic motility in six patients (see table). By contrast, both the amplitudes of segmental pressure waves and the percentage

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Subject	Mean Amplitudes (cm H_2O)			Mean Percentage Duration of Activity		
	Control	$PGF_{2\alpha}$	After $PGF_{2\alpha}$	Control	$PGF_{2\alpha}$	After $PGF_{2\alpha}$
1	7·9	6·3	6·3	41	31	30
2	10·1	21·3	14·4	40	19	68
3	8·7	5·3	8·0	21	21	28
4	9·3	8·9	5·2	36	29	19
5	9·9	15·3	10·0	7	18	28
6	11·3	5·0	6·9	19	16	13

Table *Mean amplitude of colonic pressure waves and percentage duration of pressure activity in six patients before, during, and after intravenous prostaglandin*

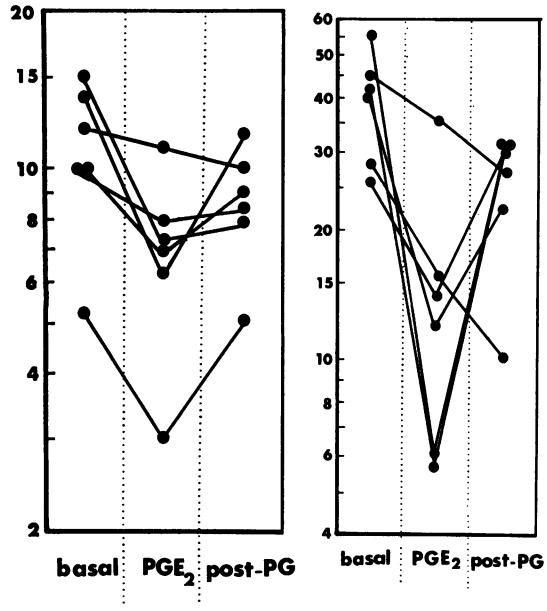

Fig *Mean amplitude (cm H_2O) of colonic pressure waves (left) and percentage duration of pressure activity (right) in six patients during and after intravenous prostaglandin$_2$.*

duration of pressure activity were significantly diminished by PGE_2 given to six other patients at 0·08 μg kg^{-1} min^{-1} for 20 min ($P < 0·05$). The mean amplitude of segmental contractions was reduced in five of the six patients and the percentage duration of activity was shortened in all six. During the post-PG period neither variable of motility differed significantly from control levels ($P > 0·05$, see fig.).

Four of the patients given $PGF_{2\alpha}$ experienced mild abdominal cramps during the PG infusion, but these were not associated with changes in the pressure record or with diarrhoea. None of the patients given PGE_2 reported any side effects.

Discussion

The inhibition by PGE_2 of colonic segmental activity is unlikely to be secondary to altered absorptive function of the small intestine, which is much slower to develop at the dose levels used in this study (Cummings, Newman, Misiewicz, Milton-Thompson, and Billings, 1973; Milton-Thompson, Cummings, Newman, Billings, and Misiewicz, 1975). Prostaglandin E_2 inhibits basal and pentagastrin-stimulated gastric acid secretion (Newman, Prado, Philippakos, and Misiewicz, 1975). Exogenous or endogenous CCK stimulates segmental colonic contractions (Harvey and Read, 1973a and b), so that a decrease in stimuli releasing CCK could lead to inhibition of colonic segmentation. It is most likely, however, that the inhibition is due to primary action of PGE_2 on the colon.

Our observations *in vivo* agree with data reported by Bennett and Posner (1971) on isolated circular human gut muscle. The present results show that changes in colonic segmentation similar to those often present in diarrhoeal states are produced by low intravenous doses of prostaglandin E_2. Our recording system does not detect changes in the tone of longitudinal muscle, but this muscle layer is contracted by PGE_2 *in vitro* (Bennett and Posner, 1971). Increased local synthesis of PG might occur in inflammatory bowel disease, eg, ulcerative colitis, and it is conceivable that PGs of the E group may play a part in the pathogenesis of the shortened and smooth colon in this condition. It is interesting to note that sulphasalazine has been shown to be an inhibitor of PG synthetase (H. O. J. Collier, personal communication).

Oral PGE_1 produces watery stools and accelerated transit through the small and large intestine (Misiewicz, Waller, Kiley, and Horton, 1968). Intraluminal PGE_1 or intravenous PGE_2 stimulate secretion of fluid into the jejunum and increase the rate of ileal flow, respectively (Matuchansky and Bernier, 1973; Milton-Thompson *et al*, 1975). Colonic absorptive function is not markedly affected by intravenous PGE_2 (Milton-Thompson *et al*, 1975), but the inhibition of colonic segmental contractions by locally produced PGE might facilitate the onward propulsion of contents by mass movements and thus contribute to the diarrhoea.

Inhibition of small intestinal segmental contractions by $PGF_{2\alpha}$ (Cummings *et al*, 1973) occurs at dose levels which in this study had no effect on the colon. The colon is also less sensitive than the lower oesophageal sphincter, which contracts in response to one tenth of the present dose of prostaglandin $F_{2\alpha}$ (Dilawari, Newman, Poleo, and Misiewicz, 1973). Isolated human colonic muscle is contracted by $PGF_{2\alpha}$ (Vanasin, Greenough, and Schuster, 1970; Bennett and Posner, 1971). The role of $PGF_{2\alpha}$ in the control of colonic motility is more conjectural, however, because this PG has not been isolated from human alimentary tissue.

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