Inhibition of canine duodenal interdigestive myoelectric complex by nutrient perfusion of jejunal and ileal Thiry-Vella loops

J C SCHANG, F ANGEL, A LAMBERT, F CRENNER, M APRAHAMIAN, AND J F GRENIER

From the Pavillon Chirurgical B, Hospices Civils, Strasbourg, France

SUMMARY The mechanisms by which the intestinal interdigestive myoelectric complex (IDMEC), recurring at about 90 minute intervals in the fasted dog, is disrupted by feeding remain unknown. We investigated whether the IDMEC could be disrupted in the duodenum by perfusing a Thiry-Vella loop with glucose in the dog. An intestinal Thiry-Vella loop, measuring one half (80 to 160 cm) of the total length of the small bowel was constructed in four dogs from the jejunum, and in four other dogs from the ileum. Extracellular nichrome electrodes were sewn on the duodenum for recording the electrical activity of the intestine. After three weeks' recovery, electrical recordings were performed in the fasted dogs in order to observe whether the IDMEC persisted in the duodenum when the Thiry-Vella loops were perfused, at different days, for four hours with solutions made of either (1) NaCl 154 mM, (2) NaCl 308 mM, (3) glucose 300 mM, or (4) glucose 600 mM, at a rate of 8 ml/min. NaCl 308 mM and glucose 600 mM were also delivered at a rate of 4 ml/min. Glucose output from the Thiry-Vella loops was measured throughout the experiments over consecutive five minute intervals. Each experiment was performed three times in each dog. The results showed that perfusing the Thiry-Vella loops with NaCl 154 mM or NaCl 308 mM did not suppress the IDMEC in the duodenum whether the flow rate was 4 or 8 ml/min. On the contrary, perfusing the jejunal loops with glucose 300 mM disrupted the IDMEC in 54% of the experiments; perfusing glucose 600 mM disrupted the IDMEC in 83% of the experiments. In the ileal Thiry-Vella loop experiments, the IDMEC was disrupted in 33% of the cases with glucose 300 mM and in 66% of the cases with 600 mM. No significant difference was observed with glucose 300 mM delivered at a rate of 8 ml/min and glucose 600 mM delivered at a rate of 4 ml/min. Finally, the inhibitory effect of perfusing the Thiry-Vella loops with glucose increased as the amount of absorbed glucose increased. These results indicate that interruption of the IDMEC by feeding probably involves extraintestinal factors. These factors do not seem to be specific for any one part of the small intestine, but they seem to be activated by intestinal absorption.

The interdigestive myoelectric complex (IDMEC) has been well documented over the last few years. This cyclic pattern of the electric spiking activity of the small bowel was first described by Szurszewski¹ in dogs. The myoelectric complex occurs only in the fasting state and consists of four sequential phases recycling regularly at about 90 minute intervals. Phase I is characterised by the

absence of spike potentials. Phase II consists of irregular spiking activity. Phase III is a short period, lasting about five minutes, during which the maximal rate of spiking activity is reached. Finally, phase IV is a transition between regular spiking activity and quiescence.

Feeding interrupts the IDMEC for several hours and induces a pattern of irregular, intermittent spiking activity. This postfeeding activity demonstrates considerable change from one nutrient to another.^{2,3} The reappearance of phase III marks

the end of the period of IDMEC interruption and regularly recurring cycles continue thereafter.

The mechanisms which control the postfeeding disruption of the IDMEC are incompletely understood. Previous work has shown that necessary requirement for interruption of the IDMEC by nutrient meals was the contact of the intestinal mucosa with these meals,¹ intravenous feeding being without effect on the IDMEC.² However, little information is available about the pathways through which mucosal contact with the nutrients leads to the interruption of the IDMEC. The purpose of our work was to determine whether perfusion of canine jejunal or ileal Thiry-Vella dogs with different nutrient solutions would alter the IDMEC in the duodenum.

Methods

EXPERIMENTAL PREPARATION

This study was carried out on eight dogs weighing 14 to 16 kg. They were anaesthetised with sodium thiopental (30 mg/kg) and a caeliotomy was performed. The small intestine was measured from the ligament of Treitz to the ileocaecal junction. Then, the bowel was transected midway between the ligament of Treitz and the ileocaecal junction. In four dogs, the jejunum was also divided 10 cm distal to the ligament of Treitz and the intervening segment of jejunum was fashioned into a Thiry-Vella (TV) loop (fig 1). In the other four dogs, the terminal ileum was divided 10 cm proximal to the ileocaecal junction and the intervening segment of ileum was fashioned into a Thiry-Vella loop. In all dogs, the intestinal continuity was re-established by end-to-end anastomosis. Four pairs of Nichrome wire electrodes were sewn to the serosa of the duodenum at 5 cm intervals. The other ends of the wires were tunneled subcutane-

Fig. 1 Experimental preparation; E1, E2, E3 are electrodes on the duodenum; LT is the ligament of Treitz.

ously and brought out in the interscapular region. No electrode was placed on the Thiry-Vella loop. The dogs were allowed three weeks' recovery before experiments were started.

ELECTRICAL RECORDINGS

The electrical recordings were obtained by connecting the electrodes to an eight-channel Beckman R 411 Dynograph recorder. Such a tracing is shown in Fig. 2, which represents the three phases of the myoelectric complex. The signals were amplified through R-C coupled amplifiers with a time constant of 0.01 second. The electrical

Fig. 2 Electrical tracing recorded from two electrodes, 3 cm apart on the duodenum of a fasted dog. Phases I, II, and III of the myoelectric complex are easy to recognise. Phase IV is not mentioned because it does not appear clearly on this particular tracing.

signals recorded from each electrode were also processed through an on-line analysis system working on real time. This system⁶ allowed us to count automatically the number of slow waves, as well as the number of slow waves superimposed with spike potentials. Each slow wave bearing spikes was indicated by a marker on the graphic record.

PERFUSATES

Control recordings were performed in the absence of perfusion. Other recordings were made while perfusing the Thiry-Vella loops, at different days, with one of the following solutions: (1) NaCl 154 mM; (2) NaCl 308 mM; (3) glucose 300 mM; and (4) glucose 600 mM. The solutions were perfused continuously at a rate of 8 ml/min, which is in the range of the flow rate in the canine jejunum after feeding a standard meal.⁷ NaCl 308 mM and glucose 600 mM were also infused at a constant rate of 4 ml/min. The length of the period of infusion was four hours (Fig. 3).

Fig. 3 Conduct of the experiment: at least one cycle of the IDMEC (with phases I, II, and III) was recorded before the perfusion of the Thiry-Vella loop was done for four hours, α indicates the time elapsing between the end of the perfusion and the reoccurrence of phase III of the IDMEC.

Perfusions were performed by inserting a polyethylene tube with an occluding balloon in the proximal stoma of the Thiry-Vella loop. The perfusion rate was controlled with a pump (Gilson Minipuls 2). The effluent from the other end of the Thiry-Vella loop was collected at five minute intervals.

At the end of the perfusion period the Thiry-Vella loop was washed out by irrigating with a solution of NaCl 154 mM at a rate of 8 ml/min for 15 minutes. This irrigation allowed us to quantify the amount of glucose remaining in the loop at the end of the perfusion period.

CONDUCT OF EXPERIMENT (Fig. 3)

Each experiment was performed on fully conscious dogs fasted for 24 hours. The dogs were allowed

to move within a cage which measured $2 \times 2 \times 2$ m. Generally, the dogs stood quietly in a corner of the cage or else slept during the experiments. The electrical activity of the duodenum was recorded in such manner that complete cycle of the IDMEC was observed. Phase III of the IDMEC was seen to migrate over the duodenum from one pair of electrodes to another. This phase was preceded by an irregular spiking activity (phase II) and followed by quiescence (phase I), thus allowing its recognition. Thirty minutes after phase III was seen in the duodenum, perfusion of the Thiry-Vella loop was begun. When the four hour perfusion was completed, the electrical recording was prolonged until phase III of the IDMEC recurred.

PARAMETERS STUDIED

IDMEC in duodenum

The main goal of this study was to determine whether the IDMEC continues to cycle in the duodenum while perfusing the Thiry-Vella loop with different solutions. Phase III of the IDMEC was accurately identified by analysing its configuration (two to five minute long period of strong spiking activity) and its caudad migration from one electrode to another.

Timing of reappearance of IDMEC

In many experiments, phase III activity was never seen during the perfusion period. In these experiments we measured the time between the end of the perfusion and the moment at which phase III of the IDMEC reoccurred. This measurement included the final washout of the loop.

Volume and glucose concentration of effluent

The volume of the effluents from the Thiry-Vella loops was measured and the concentration of glucose determined when the perfusate contained glucose. The results were expressed as the total volume output from the Thiry-Vella loop during the perfusion, and as the total amount of glucose collected during the perfusion of the loop.

STATISTICS

Three experiments with each of the perfusates were carried out in each dog. Differences in mean values were compared using the Friedman test.⁸

Results

The results are summarised in the Table.

CONTROL TRACINGS

Control tracings were obtained three weeks after the operation in the absence of perfusion. These

Table Results obtained by perfusing jejunal and ileal Thiry-Vella loops

Experiments per 4 dogs (no.)	NaCl			Glucose			Controls; no perfusion
------------------------------	------	--	--	---------	--	--	--

*Concerns only the experiments during which no phase III was observed.

Volume of TV loop effluents indicates the difference between the volume introduced into the loop and that collected from the loop. $\oplus$ indicates secretion of water from the loop. $\ominus$: significantly different at $p < 0.05$ from controls and NaCl experiments.

experiments showed a regular cyclic recurrence of the IDMEC in the duodenum of all dogs. The mean period of the cycles was about 95 minutes, without difference between the four dogs with a jejunal Thiry-Vella loop and the four dogs with the ileal Thiry-Vella loop.

NaCl PERFUSIONS

Perfusion of the jejunal and ileal Thiry-Vella loops with 154 mM NaCl or with 308 mM NaCl did not significantly alter the period of regular occurrence of the IDMEC in the duodenum. Furthermore, no changes were noted when the rate of perfusion of NaCl 308 mM was 4 ml/min or 8 ml/min.

The volumes of the effluents varied with the different perfusates. With NaCl 154 mM perfused at 8 ml/min, net absorption of water occurred—that is, the volume perfused was larger than the total volume of effluents. In contrast, perfusion with NaCl 308 mM was followed by a net secretion of water that was small when the flow rate was 4 ml/min and larger when it was 8 ml/min.

GLUCOSE PERFUSIONS

Perfusion of the Thiry-Vella loops with glucose solutions consistently decreased the number of phase III seen in the duodenum. When compared with the control experiments with both the jejunal and ileal Thiry-Vella loops (25 + 25 = 50 phase III observed during 24 experiments), perfusion with glucose 300 mM at 8 ml/min was followed by a

significant ($p < 0.05$) decrease in the number of phase III (9 + 13 = 22 phase III during 24 experiments). This decrease was significantly greater when glucose 600 mM at 8 ml/min was used, only 4 + 2 = 6 phase III being observed during 24 experiments. No significant difference was noticed whether glucose at 300 mM at 8 ml/min or glucose 600 mM at 4 ml/min (7 + 14 = 21 phase III during 24 experiments) were used. However, the total number of phase III occurring during the perfusion of the jejunal loops with all glucose solutions (9 + 7 + 2 = 18 phase III observed during 36 experiments) was significantly ($p < 0.001$) smaller than the number of phase III observed when ileal loops were perfused (13 + 14 + 4 = 31 phase III observed during 36 experiments).

The net amount of glucose absorbed from both the jejunal and ileal Thiry-Vella loops was larger with glucose 600 mM at 8 ml/min (932 + 670 = 1602 mM) than with 600 mM at 4 ml/min (548 + 378 = 926 mM). No significant difference was noticed between glucose 300 mM at 8 ml/min and glucose 600 mM at 4 ml/min. Finally, the amount of glucose absorbed from the jejunal Thiry-Vella loops (445 + 548 + 932 = 1925 mM) was larger ($p < 0.05$) than that absorbed from the ileal Thiry-Vella loops (310 + 378 + 670 = 1358 mM).

COMPLETE INHIBITION OF DUODENAL IDMEC

No phase III of the IDMEC was observed in 6 + 4 = 10 out of 24 experiments when both the jejunal

and ileal Thiry-Vella loops were perfused with glucose 300 mM at 8 ml/min, and in 7+4=11 out of 24 experiments when glucose 600 mM at 4 ml/min was perfused. Phase III were not seen in 10+8=18 out of 24 experiments when glucose 600 mM at 8 ml/min was used.

Perfusion of the jejunal Thiry-Vella loops with all glucose solutions was associated with the absence of phase III in 6+7+10=23 out of 36 experiments, while 4+4+8=16 out of 36 experiments when the ileal Thiry-Vella loops were perfused.

During the period of IDMEC inhibition, the pattern of myoelectrical activity in the duodenum was made of spike potentials superimposing 20 to 25% of the slow waves, indicating a post-feeding pattern.

In these cases the IDMEC did not reoccur immediately after the end of the perfusion period, despite the fact that washout of the perfusate cleared the loops within five minutes of any remaining glucose in the lumen. When glucose 300 mM at 8 ml/min or glucose 600 mM at 4 ml/min were perfused, the first phase III was observed to reoccur after 30 to 45 minutes, while the delay reached 60 to 90 minutes when glucose 600 mM at 8 ml/min was perfused.

Discussion

The results obtained in our study show that the IDMEC is inhibited by feeding through extra-intestinal mechanisms, at least partly. Indeed, no intraluminal continuity was left between the Thiry-Vella loop and the duodenum so that the inhibitory effects must have been driven through central—neural or humoral—pathways. The precise nature of these mechanisms is not known. However, our study shows that these mechanisms are not specific to any one part of the small bowel, because the IDMEC was disrupted in the duodenum by perfusing nutrients in either a jejunal or an ileal Thiry-Vella loop.

These extraintestinal non-specific mechanisms do not seem to be significantly influenced by the flow rate or osmolality of the solutions introduced in the Thiry-Vella loops. In the NaCl experiments, IDMEC was not altered by changes in net absorption or net secretion of water. No significant difference was observed whether the flow rate of the solutions was 4 or 8 ml/min. In the glucose experiments, the same effects were observed with either glucose 300 mM at 8 ml/min or glucose 600 mM at 4 ml/min, while these experiments differed by the flow rate as well as by the fact that a secretion

of water occurred with glucose 600 mM at 4 ml/min and an absorption of water occurred with glucose 300 mM at 8 ml/min.

On the contrary, the inhibitory factors released from the Thiry-Vella loop seemed to depend, at least partly, on glucose absorption in the Thiry-Vella loop. Previous investigators have shown that the interruption of the IDMEC after feeding dogs orally could be related to both the biochemical nature of the food components and the caloric load of the meal.^{2,3} Moreover, other workers have reported that changes in intestinal absorption of a given meal—for instance, by introducing fat directly into the jejunum in the absence of bile salts—could result in subsequent changes in the duration of interruption of the IDMEC.⁴ These observations suggest that IDMEC inhibition is related with intraluminal absorption of nutrients. However, in our study, we observed that, when the IDMEC was abolished completely during four hours of glucose perfusion, a considerable time elapsed before IDMEC reappeared. Therefore, the IDMEC was inhibited even though no glucose remained in the lumen of the Thiry-Vella loop. These findings suggest that the duration of IDMEC inhibition was longer than the duration of mucosal contact with the glucose containing perfusate.

Finally, the observations reported in the present study can be put together with previous findings having shown that the IDMEC could be interrupted in a Thiry-Vella loop while feeding a dog orally.¹⁰ This suggests that IDMEC interruption results from a two-way system, with a sensitive end in the mucosa of the bowel and an efferent end in the intestinal smooth muscle. Between these two ends, inhibitory informations and orders are transmitted through mechanisms which can be of neural or humoral nature. Nervous mechanisms may play a role through nerve endings situated in the bowel wall which are known to be sensitive to many biochemical stimuli.^{11,12} However, section of neural pathways such as the vagus¹³ or the splanchnic nerves¹⁴ did not demonstrate considerable change in the inhibition of the IDMEC after feeding. Hormonal mechanisms are now thought to play a major role, since infusion of several hormones—insulin,¹⁵ CCK,¹⁶ gastrin¹⁷—has been shown to inhibit the myoelectric complex. However, the responsibility of any one of these hormones remains to be clearly identified.

We would like to thank Dr M Sarr (Mayo Clinic, Rochester, Minnesota, USA) for his aid and his helpful suggestions in writing this article.

References

- ¹Szurszewski JH. Migrating electric complex of the canine small intestine. *Am J Physiol* 1969; **217**:1757-63.
- ²De Wever J, Eeckhout C, Vantrappen G, Hellemans J. Disruptive effects of test meals on interdigestive motor complex in dogs. *Am J Physiol* 1978; **235**: E661-E5.
- ³Schang JC, Sava P, Angel F, Lambert A, Grenier JF. Specific effects of different food components on intestinal motility. *Eur Surg Res* 1978; **10**:425-32.
- ⁴Deweever I, Eeckhout C, Vantrappen G, Hellemans J. How does oil disrupt the interdigestive myoelectric complex? In: Christensen J, ed. *Gastrointestinal motility*. New York: Raven Press, 1980; 295-8.
- ⁵Weisbrodt NW, Copeland EM, Thor PJ, Dudrick SJ. Small bowel motility during intravenous hyperalimentation in the dog. *Gastroenterology* 1975; **68**: A154/1011.
- ⁶Crenner F, Lambert A, Schang JC, Angel F, Grenier JF. Analog automated analysis of small intestinal electromyogram. *Med Biol Eng Comp* 1980; (In press.)
- ⁷Fordtran JS, Ingelfinger FJ. Absorption of water, electrolytes, and sugars from the human gut. In: Code CF, ed. *Handbook of physiology*, section 6, volume 3. Baltimore: Williams and Wilkins, 1968; 1457-90.
- ⁸Bueno L, Fioramonti J, Ruckebusch M. Rate of flow of digesta and electrical activity of the small intestine in dogs and sheep. *J Physiol (Lond)* 1975; **249**:69-85.
- ⁹Lehmann EI. *Non-parametric statistical methods based on ranks*. San Francisco: McGraw-Hill, 1975.
- ¹⁰Schang JC, Sava P, Dauchel J, Angel F, Grenier JF. Relation entre motricité et absorption intestinales. *Pathol Biol (Paris)* 1977; **27**:389-93.
- ¹¹Hunt JN. The site of receptors slowing gastric emptying in response to stretch in test meals. *J Physiol (Lond)* 1960; **154**:270-6.
- ¹²Sharma KN, Nasset ES. Electric activity in mesenteric nerves after perfusion of gut lumen. *Am J Physiol* 1962; **202**:725-30.
- ¹³Marik F, Code CF. Control of the interdigestive myoelectric activity in dogs by the vagus nerves and pentagastrin. *Gastroenterology* 1975; **69**:387-95.
- ¹⁴Marlett JA, Code CF. Effect of celiac and superior mesenteric ganglionectomy on interdigestive myoelectric complex in dogs. *Am J Physiol* 1979; **237**: E432-E436.
- ¹⁵Bueno L, Ruckebusch M. Insulin and jejunal electrical activity in dogs and sheep. *Am J Physiol* 1976; **230**:1538-44.
- ¹⁶Mukhopadhyay AK, Thor PJ, Copeland EM, Johnson LR, Weisbrodt NW. Effect of cholecystokinin on myoelectric activity of small bowel of the dog. *Am J Physiol* 1977; **232**:E44-E47.
- ¹⁷Thomas PA, Schang JC, Kelly KA, Go VLW. Can endogenous gastrin inhibit canine interdigestive gastric motility? *Gastroenterology* 1980; **78**:716-21.