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Small bowel resistances and the gastroduodenal brake

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SUMMARY Osmoreceptors in the upper small bowel may delay gastric emptying by inhibiting fundal tone and/or by increasing outflow resistances. In this study we examined the contribution of postpyloric resistances to this braking system. Seven dogs had gastric emptying of 250 ml 15% dextrose, labelled with ^{99m}Tc-DTPA, measured by gamma camera imaging (preoperative studies: n=21). A proximal duodenal cannula was inserted and studies repeated in four modes: with the cannula closed (n=14); with total diversion of gastric effluent through the cannula (n=7); with diversion and downstream reinstillation of effluent at a constant rate (n=14) equivalent to emptying calculated from studies without diversion; and with diversion and total reinstillation of effluent (n=14). Gastric emptying at 90 minutes was similar in preoperative studies (48±5% – mean±SEM) and in those with the cannula closed (50±3%). By comparison 'total diversion' produced rapid emptying over 90 minutes (97±1%; $p<0.001$). Reinstillation of effluent at a constant rate reduced the 90 minute emptying to 59±6%, and total reinstillation slowed emptying further to 37±4% ($p<0.05$). Neither reinstillation protocol yielded gastric emptying rates that were significantly different from those in studies without diversion. With total reinstillation, emptying and hence reinstillation rates were more variable, proceeding in a step and plateau fashion. We conclude that canine jejunal osmoreceptor activity is mediated through the stomach, with postpyloric resistances playing little or no role. Gastric emptying curve analysis suggested that increments of rapid small bowel filling provoke exaggerated braking responses.

Gastric emptying of hypertonic liquids is thought to be regulated by osmoreceptors which are situated in the duodenum[1] and jejunum[2] of man and in the jejunum[3] of the dog. The mechanism by which this is brought about is, however, incompletely understood. Theoretically, emptying could be retarded in three ways. First the tone in the gastric fundus could be diminished, decreasing intragastric pressure and reducing the expulsive force. Second the diameter of the antropyloric segment could be reduced, providing a gastric outflow resistance. Finally the tone in the upper small bowel could be increased, generating a postpyloric outflow resistance.

There is some evidence to suggest that each of these three actions occur,[4] but their relative contributions to the braking system are unknown. In this study we investigated the role of postpyloric resistances in the control of gastric emptying of liquids, in dogs. The study was based on the assumption that total diversion of gastric effluent through a proximal duodenal cannula, combined with distal duodenal reinstillation of cannula effluent, will release postpyloric resistances to gastric emptying while maintaining jejunal osmoreceptor activity.

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Methods

DOGS

Seven Beagle bitches (weights 12–17 kg) were trained to stand in a Pavlov sling against a Nuclear Enterprises 8900 gamma camera. Sedatives were not used. Food was withheld for 16 hours and water for 4 hours before starting each study. Two hundred and fifty millilitres 15% dextrose labelled with 10 MBq ^{99m}Tc-DTPA was then instilled into the stomach *via* an orogastric tube. Instillation took place over 90 seconds and after this the tube was removed. Imaging proceeded over 90 minutes with a 90 second frame time and the data acquired from each study were stored on floppy disc for subsequent analysis. Each frame was corrected for movement, in both the horizontal and vertical planes, by means of a novel image alignment programme (to be detailed in a seperate publication). A gastric region of interest was defined on the second frame and an intragastric time-activity curve was generated for the entire period of imaging. The image alignment programme also facilitated correction for small bowel encroachment into the gastric region of interest. Curves were corrected for isotope decay and, when appropriate, correlation coefficients for linear fits were obtained using a computer programme.

Each dog had three preoperative studies to assess reproducibility and individual daily variation in emptying rates. After this a Thomas cannula was inserted into the duodenum, approximately 4 cm from the pylorus (Fig. 1). A cuff of Dacron 1·5 cm long was sutured loosely around the duodenum immediately distal to the cannula. The animals were then allowed six to eight weeks to recover. After this a further series of studies was completed on each animal over a three to four week period. All animals remained well and maintained their body weight.

Two studies with the cannula closed were carried out on each dog. The results of these studies were compared with the preoperative results and a mean emptying rate then calculated for each animal from the results of all five studies without diversion (three preoperative plus two studies with the cannula closed).

In subsequent studies, with the cannula open, a 12FG Foley catheter was inflated to occlude the bowel lumen at the site of the cuff (Fig. 1). This allowed effluent to be totally diverted through the cannula and also permitted reinstillation of cannula effluent into the distal duodenum. After catheter insertion, 1 ml dilute methylene blue solution was instilled distally to ensure a complete seal by the balloon. A 15 minute rest period was then allowed, before beginning the studies. Reinstillation was carried out manually, refilling a syringe with effluent and maintaining an even rate of infusion throughout each five minute period of the study.

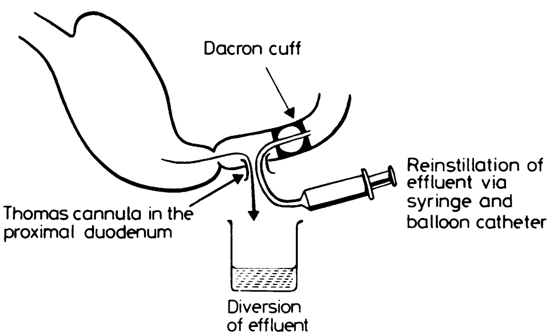

Fig. 1 *Diagram of the experimental model.*

Single studies were performed with total diversion of effluent without distal reinstillation. Each dog then had two studies with diversion and distal reinstillation of effluent at a constant rate equal to that animal's mean gastric emptying rate, calculated from its initial five studies without diversion. At the start of these studies, an equivalent amount of 15% dextrose was infused distally until an adequate volume of effluent had accumulated for reinstillation over the next five minute period.

Finally each dog had two studies in which effluent was diverted and all effluent collected over each five minute period was then totally reinstilled, at an even rate over the next five minute period, repeating this sequence throughout the duration of the study.

STATISTICAL ANALYSIS

Comparisons of the amounts emptied over 90 minutes were made using Student's paired *t* test. For the duplicated studies the mean values for each animal were paired and were used to calculate the standard errors for the cohort.

Results

Preoperative gastric emptying was well characterised by linear functions (r=0·90–0·99: mean=0·97). Gastric emptying at 90 minutes, calculated from the scintigraphic data, was 48±5% (mean±SEM). The overall range of emptying at 90 minutes was 19–78%. The individual variation in the amounts emptied in the three preoperative studies was 3–19%, with a mean of 12%. In studies with the cannula closed emptying was also linear (r=0·96–0·99: mean=0·98). Emptying at 90 minutes was 50±3% (range: 35–61%; mean individual variation=8%). There were no statistically significant differences in emptying at any time between these two groups of studies (Fig. 2) and the results were combined to produce a mean emptying curve for studies without diversion.

The results of studies with diversion of gastric effluent are shown in Figure 3. Gastric emptying curves for studies with total diversion of effluent, without reinstillation, showed precipitous emptying so that most of the test meal had emptied by 30 minutes. Emptying at 90 minutes (97±1%) was significantly greater than for the studies without diversion ($p<0·001$).

Reinstillation of effluent at a constant rate, equivalent to the individual animal's normal rate of gastric emptying, calculated from studies without diversion, caused a marked delay compared with total diversion without reinstillation. Emptying at 90 minutes after

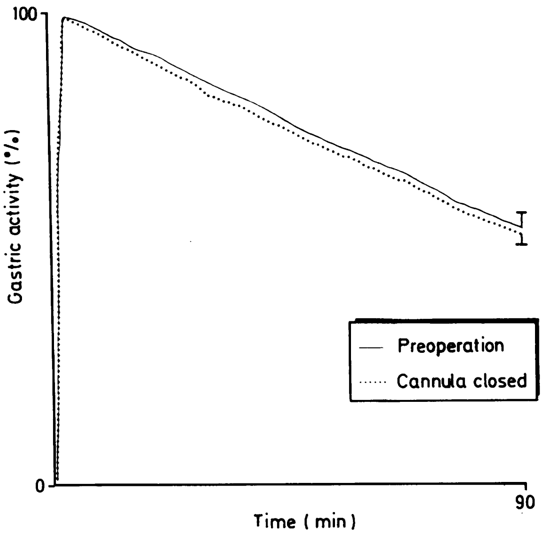

Fig. 2 *Results of studies without diversion. Gastric activity, expressed as a percentage of peak gastric activity, is plotted on a linear scale against time, for preoperative (n=21) and postoperative studies with the cannula closed (n=14). Curves represent mean values, with the SEM at 90 minutes as shown. Ranges of emptying at 90 minutes were 19–78% for the preoperative studies and 35–61% for those with the cannula closed.*

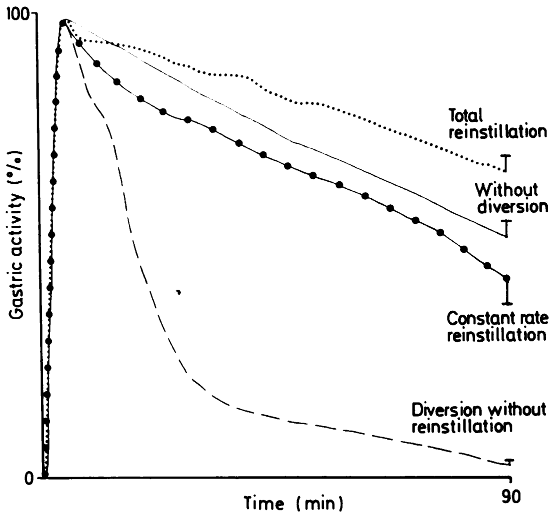

Fig. 3 *Plots of gastric activity against time for the different protocols used. Studies with diversion without reinstillation (n=7) gave greater emptying at 90 minutes than studies (n=35) without diversion (97±1% v 49±4%: p<0·001). Studies with total reinstillation (n=14) produced less emptying than those (n=14) with reinstillation at a constant rate (37±4% v 59±6%: p<0·05). Neither reinstillation protocol produced results that were significantly different from studies without diversion.*

constant rate reinstillation was 59±6% (mean individual variation=23%). This was not significantly different from emptying in studies without diversion.

When all effluent, for each five minute period, was totally reinstilled over the next five minute period an even greater delay in emptying occurred, except over the initial 10–15 minutes. Emptying at 90 minutes was 37±4% (mean individual variation=12%). These results were not significantly different from those obtained in studies without diversion. However, with 'total reinstillation' gastric emptying was significantly slower ($p<0·05$) than when effluent was reinstilled at a constant rate. Studies with 'total reinstillation' of effluent produced gastric emptying curves that showed short step and long plateau phases (Fig. 4), while smooth patterns of emptying were observed in studies without diversion and in those with reinstillation at a constant rate.

Discussion

The mechanism of the gastroduodenal brake has been examined previously by measuring the gastric[5,6] or pyloric[7,8] pressure responses to various test meals and also by assessing gastric emptying of test meals while maintaining a constant intragastric pressure.[9] While the results of these studies have been conflicting, a significant role for postpyloric resistances has been inferred by more than one group of investigators.[5,9] The demonstration of gastric outflow resistances while maintaining a constant positive intragastric pressure, however, may be a consequence of unphysiological conditions.

Although much of our present knowledge of gastric physiology is based on studies upon dogs, there is little information on the normal variation of

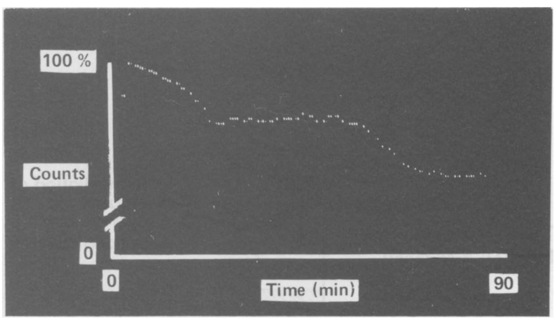

Fig. 4 *An individual example of a study with total reinstillation of effluent. Note the plateau phases following episodes of rapid gastric emptying.*

gastric emptying in this animal. As in man, canine gastric emptying rates vary with different test meals, a meal that empties slowly being associated with a wider range of emptying rates.[10 11] In the present study, preoperative variations exhibited by individual animals, expressed in relationship to the range for all animals, were of a similar magnitude to those reported in man after a saline test meal.[10] In our study we have tried to reduce the influence of normal variation by basing our analysis on mean values of duplicate studies, except for the studies with total diversion without reinstillation in which emptying was almost complete at 90 minutes in all animals. Although isotonic liquids may empty in the pattern of a single exponential, we have observed in man that increasing the osmolarity of a test meal causes a shift towards linearity (unpublished data). Linear correlation coefficients were found to be better than single exponential correlation coefficients for preoperative studies. Similarly in man gastric emptying of 15% dextrose has been reported to be linear.[12] Gastric emptying is slower in the dog than in man, although when expressed in terms of meal energy emptied per unit of body weight, emptying in this study was approximately 4 cal/kg/h. This compares with an approximate value of 3 cal/kg/h which has been reported for lean man.[4] The difference may possibly reflect the higher basal metabolic rate in the dog.

Gastric and duodenal cannulae have been widely used in experimental studies of upper gastrointestinal motility and secretion. Despite this, the effects of cannulae on gastric emptying have not been reported. In this study, the insertion of a duodenal cannula with a Dacron cuff appeared to cause no disturbance to the rate and pattern of gastric emptying, although there was some narrowing of the overall range. Possibly this reflects upon the dogs becoming more accustomed to the scanning procedure.

Our interpretation of the postoperative studies is based on the assumption that in studies with the cannula closed, osmoreceptors in the upper small bowel are stimulated and emptying is subject to both gastric and small bowel braking influences. With total diversion osmoreceptors are not stimulated and braking influences are absent. With diversion and distal reinstillation osmoreceptors are stimulated, but since the cannula drains freely the system is no longer influenced by small bowel resistances and any delay in gastric emptying must therefore be effected by gastric components. In studies in which effluent was reinstilled at a constant rate, calculated to be equivalent to that animal's normal rate of gastric emptying, our aim was to challenge jejunal osmoreceptors with an osmotic stimulus identical to that provided in studies without diversion. Dextrose was chosen as the test meal because intraduodenal hypertonic dextrose has been shown to inhibit gastric acid secretion,[13] while being a weak stimulus of pancreatic and biliary secretion.

In these studies reinstillation of effluent at the calculated normal rate restored the braking response to near normal. The result suggests that gastric components of the braking system predominate, small bowel resistances having little or no role under these test conditions. It could be argued that our estimation of the volume of gastric effluent entering the duodenum during studies without diversion, being based on the test meal volume and the fractional decrease in gastric radioactivity, was an underestimate because of dilution of the test meal by gastric secretion. Small amounts of pancreaticobiliary secretion could have increased this dilution, as the major duodenal papilla was proximal to the occluding duodenal balloon. Were this so, under-reinstillation of effluent may have accounted for the small difference in results between studies with reinstillation of effluent at a constant rate and those without diversion. An alternative explanation might be sought in the possible augmentation of the gastroduodenal pressure gradient produced by opening the proximal duodenum to the atmosphere. We have not accounted for this factor, but in retrospect our results would appear to indicate that it could not have been a major influence.

To address the possibility of dilution of the test meal, studies were carried out using an alternative protocol with reinstillation of the total cannula effluent. In these studies, however, emptying patterns were irregular, exhibiting a combination of rapid and slow phases. We suspect that initial periods of rapid emptying resulted from the brief interruption of the normal enterogastric feed back, there being a five minute phase difference between gastric emptying and subsequent osmoreceptor stimulation. Interestingly, studies with total reinstillation of effluent produced significantly slower gastric emptying than that seen in studies with reinstillation at a constant rate, even though the overall volume of instillate was smaller in the former studies. This is difficult to explain without postulating that increments of rapid jejunal filling provoked exaggerated braking responses, mediated by gastric components of the braking mechanism. At times, we noted that episodes of relatively rapid small bowel filling temporarily caused complete inhibition of gastric emptying. It is unclear, from this study, whether rapid small bowel filling delayed gastric emptying by excessive osmoreceptor stimulation, or by invoking an inhibitory response to distension mediated by the sympathetic nervous system. As a clinical correlate we note that after gastric surgery, patients may develop symptoms attributable to a combination of rapid gastric emptying and to gastric stasis.[14] Gastric stasis occurring after truncal vagotomy has been attributed to deficient antral grinding of solids.[15] The results of this study may point to a further reason for symptoms of stasis, since an initial phase of rapid emptying is normal after ulcer surgery.

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