Role of cholecystokinin in the gastric motor response to a meal in horses

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Objective—To measure plasma cholecystokinin (CCK) activity and the effect of a CCK-1 receptor antagonist on accommodation of the proximal portion of the stomach, and subsequent gastric emptying, in horses after ingestion of high-fat or high-carbohydrate meals.

Animals—6 healthy adult horses with gastric cannulas.

Procedures—In the first study, horses were offered a high-fat (8% fat) or a high-carbohydrate (3% fat) pelleted meal of identical volume, caloric density, and protein content. Related plasma CCK-like activity was measured by radioimmunoassay (RIA). In a separate experiment, a horse was fed a grain meal with corn oil and phenylalanine, and plasma CCK activity was assessed by bioassay. A second study evaluated the effect of a CCK-1 receptor antagonist, devazepide (0.1 mg/kg, IV), on gastric accommodation and emptying following a meal of grain supplemented with either corn oil (12.3% fat) or an isocaloric amount of glucose (2.9% fat). Gastric tone was measured by a barostat and emptying by the 13C-octanoic acid breath test.

Results—No plasma CCK-like activity was detected by RIA or bioassay before or after ingestion of meals. Preprandial devazepide did not alter the gastric accommodation response but did significantly shorten the gastric half-emptying time and time to peak breath 13CO2 content with the glucose-enriched meal.

Conclusions and Clinical Relevance—In horses, CCK participates in regulating the gastric motor response to a meal. Compared with other species, horses may be more responsive to carbohydrate than fat. A vagovagal reflex most likely mediates this regulation, with CCK as a paracrine intermediary at the intestinal level. (Am J Vet Res 2006;67:1998–2005)

Regulation of gastric motility in response to consumption of a meal is the first step of a long and complex series of events aimed to maximize the digestion and absorption of nutritional components of the diet. Different neural and humoral pathways involved in this regulatory system are initiated after ingested nutrients interact with chemical receptors localized within the intestinal wall. One of the key components in these regulatory pathways is CCK.

Cholecystokinin is a peptide released from intestinal endocrine cells in response to food intake and is known to regulate motility, pancreatic enzyme secretion, gastric emptying, and gastric acid secretion in a variety of species. For instance, it is well recognized that the fat-induced feedback inhibition of gastric emptying is mediated, at least in part, by the release of CCK from the intestinal mucosa. The mechanism of action is unclear, but it seems that its main effect is relaxation of the proximal portion of the stomach. Cholecystokinin also delays gastric emptying by stimulating contractions of the pyloric sphincter and the proximal portion of the duodenum, thus increasing the resistance to gastroduodenal flow of chyme.

The effects of CCK are mediated via 2 G-protein coupled receptors, termed CCK-1 and CCK-2 receptors. Although the CCK-1 receptor binds to sulfated CCK with a 500- to 1,000-fold higher affinity than to gastrin, the CCK-2 receptor interacts with gastrin and CCK with almost the same affinity. The CCK-1 or A (for alimentary) receptor is primarily localized to the gastrointestinal system, whereas the CCK-2 or B (for brain) receptor is found within the CNS. Both receptor types are highly conserved, having 70% to 80% amino acid identity between receptors among various species.

Different approaches have been used in other species to determine the importance of CCK in the nutrient-induced feedback regulation of gastric motility. A traditional approach has been to measure the release of CCK into the circulatory system in response to ingestion or duodenal infusion of various nutrients. Plasma CCK concentrations have not been measured in horses, and therefore, nothing is known about the ability of nutrients to stimulate CCK release from equine enteroendocrine cells. In other species, the most potent stimulants of CCK secretion are digested fat and protein, whereas CHO has little to no effect. Evidence of CCK involvement in feedback regulation has also been determined by the use of CCK receptor antagonists. Oral or systemic administration of CCK-1 receptor antagonists, such as devazepide or loxiglumide, attenuates nutrient-induced inhibition of gastric emptying in humans, rats, monkeys, cats, and dogs.
Finally, current evidence suggests that involvement of CCK in feedback regulation of gastric emptying may not always be reflected by high concentrations of plasma CCK following intake of nutrients. An increasingly accepted theory is that the presence of specific nutrients within the duodenum stimulates secretion of CCK from enteroendocrine cells within the submucosa, which in turn stimulates intestinal vagal sensory neurons in a paracrine fashion to inhibit gastric emptying by a vagovagal reflex.2 All of this suggests that endogenous CCK may act more by a paracrine or neurocrine fashion than an endocrine fashion at CCK-1 receptors.

Endocrine cells immunoreactive for CCK are present within the duodenal wall of horses,26 and CCK-2 receptors have been identified on somatostatin cells of pancreatic islets.22 Although this suggests a role for CCK receptors have been identified on somatostatin cells of the blood in EDTA tubes with and without aprotinin, b in the Materials and Methods.

To study the effect of devazepide, a selective CCK-1 receptor antagonist devazepide. An indwelling silastic gastric cannula23 had been implanted in each horse (2.5 hours). In both instances, plasma was stored at –70°C after centrifugation. Sample tubes and syringes were constantly cooled in an ice bath before and after use. Thawed plasma samples were extracted with 96% ethanol and evaporated overnight by use of a concentrator4 at 37°C. Dry extracts were dissolved to the original sample volume with a diluent provided in the kit. A recovery control with CCK-8 (amino acids 26 to 33) sulfate was included to estimate the extraction recovery. A 4-day assay was performed with rabbit antiserum raised against synthetic CCK-8 sulfate. Antibody-bound 131I-radiolabeled CCK sulfate was separated from the unbound fraction by use of double antibody solid phase.

Measurement of gastric tone—A barostat1 was used to assess changes in proximal intragastric volume and pressure, according to a method that we have previously published.25 A polyester bag of approximately 1,700-ml volume was connected to the barostat through a plastic catheter. By use of barostat software, changes in bag pressure and volume were continuously recorded and saved in a designated file. Following an experiment, the recorded data were transferred to a compact disk for the permanent record.

13C-octanoic acid breath test—Rates of gastric emptying were assessed with the 13C-octanoic acid breath test as described by Sutton et al.2 This noninvasive, nonradioactive technique is based on detection of 13C-enrichment in breath, following ingestion of a meal labeled with 13C-octanoate. This marker is rapidly and totally absorbed in the small intestine and oxidized in the liver to produce CO2. For each test, 13C-octanoic acid (1.5 mg/kg) was added to egg yolk (1 yolk/250 mg of marker), baked in a microwave oven, and thoroughly mixed into the test meal.

Test meals composition—For the plasma CCK activity studies, 2 isocaloric (1.5 kcal/kg) and nearly isovolumetric pelleted meals (10% protein) were used. The high-CHO pelleted meal was rich in starch (31%) and poor in fat (3%), whereas the high-fat pelleted meal was rich in fat (8%), had no starch, and contained more fiber (43.5% neutral detergent fiber in the high-fat meal vs 28.4% neutral detergent fiber in the high-CHO meal).

For the devazepide studies, 2 isocaloric (1.95 kcal/kg) and isovolumetric diets were formulated. A control meal of 10% protein sweet feed (1.5 kcal/kg), fed at 0.5 g/kg of BW, was used as the basis to prepare the 2 experimental diets. A high-fat meal (12.3% fat) was prepared by adding corn oil at 0.05 g/kg of BW to the control diet. A high-CHO meal (2.9% fat) was prepared by adding glucose at 0.113 g/kg of BW to the control diet.

Study design—In the plasma CCK activity studies, each horse participated in 4 experiments involving 2 sessions/diet. The sequence of the experiments was based on a 2-period randomized block design. In the first period, group A (3 horses) received the high-fat pelleted diet and group B (3 horses) received the high-CHO pelleted diet. Horses were gradually acclimated to the test diets during a 1-week period. At the end of the accommodation period, they received 5 g/kg each day of the respective test diet, divided into 2 feedings, until the completion of the first period. Horses were also fed free-choice coastal Bermuda grass hay for the entire period. After the dietary accommodation period, horses completed 2 randomly assigned studies.

In the devazepide studies, each horse participated in 4 experiments, which differed in the meal offered to the horse and treatment with or without devazepide prior to meal intake. To account for any effects of the vehicle used to dilute the devazepide, a fifth experiment was performed with the high-CHO diet but pretreatment with the vehicle alone. The sequence of the experiments was based on a randomized block design. Horses were provided 2 to 3 kg of the same sweet feed.
were collected with a modified mask fitted with a 250-mL
Duration of meal intake was also recorded. Breath samples
2 diets, and recording continued for a total of 120 minutes.
the horse was offered 1 of the
obtain a baseline volume. Then, the horse was offered 1 of the
The first 30 minutes of the experiment were recorded to
instrumentation (ie, gastric emptying coefficient, t½, and tmax) between
gastric emptying rate, was calculated according to Maes;
1 mL of distilled water, so that samples with original volume
samples with original volume and concentrated samples were assayed. Increasing concentrations of caerulein, an analog of CCK, were used as a positive control.
Dievazepide study procedure—No horse participated in >1 experiment/wk. Food was withheld for 14 hours before each experiment. After this period, the horse was placed in the stocks. A jugular catheter was placed before starting the experiment, and blood was withdrawn with chilled syringes. Samples were obtained 10 minutes before feeding and then every 15 minutes for a total of 120 minutes. Collected blood was transferred into chilled EDTA tubes with and without aprotinin, for later comparison of RIA results. Samples were centrifuged, and the plasma was stored at −70°C until CCK activity determination.
A separate single experiment was performed to collect plasma samples for an in vitro bioassay measurement. The bioassay, developed by Liddle et al., is based on the ability of bioactive CCK peptides extracted from plasma to stimulate amylase release from isolated rat pancreatic acini and is described in detail elsewhere. After withholding of food overnight, 1 horse was offered 226 g of sweet feed (0.5 kg) mixed with 30 mL of corn oil and 5 g of phenylalanine. Duplicate blood samples were obtained before the meal and 10, 20, 30, and 50 minutes after meal ingestion. Blood was collected in EDTA tubes with and without aprotinin and constantly cooled in an ice bath until the end of the collection. Plasma samples were extracted and brought to dryness, as done for the measurement of plasma CCK-like activity by RIA. Dry samples of 1-mL and 5-mL original plasma volume were shipped to the University of Sherbrooke, Canada, for bioassay of CCK activity. All samples were reconstituted with 1 mL of distilled water, so that samples with original volume and concentrated samples were assayed. Increasing concentrations of caerulein, an analog of CCK, were used as a positive control.

Devazepide study procedure—No horse participated in >1 experiment/wk. Food was withheld for 14 hours before each experiment. After this period, the horse was placed in the stocks. Once the horse was in the stocks, the gastric cannula was cleaned. The previously folded barostat bag was introduced into the stomach through the cannula. The bag was inflated manually, and its positioning within the proximal portion of the stomach was verified by an endoscope introduced nasogastrically. Correct position was defined as being above the margo plicatus. Next, the bag was emptied by a syringe and connected to the barostat by the catheter. For devazepide or vehicle administration, a 14-gauge commercially available catheter was placed into a jugular vein.
The barostat maintained a constant intragastric bag pressure of 2 ± 0.5 mm Hg. Thereafter, motor activity of the proximal portion of the stomach was recorded for 2 hours by measuring changes in volume of the isobarically controlled bag. The first 30 minutes of the experiment were recorded to obtain a baseline volume. Then, the horse was offered 1 of the 2 diets, and recording continued for a total of 120 minutes. Duration of meal intake was also recorded. Breath samples were collected with a modified mask fitted with a 250-mL aluminum-coated polyethylene bag. Before the bag was filled, the horse was allowed to breathe once through the mask and fitted with a unidirectional valve. Duplicate samples were transferred from this bag to 10-mL glass tubes, conveniently sealed, and stored until ready for stable isotope analysis. Three basal breath samples were collected 60, 15, and 5 minutes before test meal ingestion and thereafter at 15-minute intervals for 3 hours, then at 30-minute intervals for 4 hours for a total of 23 collections/experiment.

In those experiments that included treatment with devazepide, a dose of 0.1 mg/kg was administered into the jugular vein of the horse as a bolus 10 minutes prior to ingestion of any of the meals. The dose was prepared by diluting powdered devazepide in 7 mL of 90% DMSO and 13 mL of 50% dextrose. This dose had been previously used in other species without any adverse effects. To avoid the risk of hemolysis caused by IV administration of nondiluted DMSO, the bolus was administered over a period of 3 minutes. The same protocol of administration was followed in the experiments where only the DMSO-dextrose vehicle was injected.
Barostatic recording was entirely done with the horse in the stocks. Once this component of the study was finished at 120 minutes, the horse was moved into a stall and the rest of breath samples collected there. Because it was difficult to remove the intragastric bag after feeding the horse, and to avoid loss of food through the cannula, its removal was done after completion of the study. Following each experiment, the recording equipment was removed, the gastric cannula was plugged, and the horse was returned to the paddock.

Intragastric volume analysis—One bag-volume sample per second was obtained throughout the experiments. For every diet, data of the experiments were grouped into 2-minute blocks and averaged for the 5 horses. The first 15 blocks (30 minutes) were used to obtain a baseline bag volume. The remaining blocks (90 minutes) corresponding to the postfeeding period were analyzed to study the relaxation response of the proximal portion of the stomach in relation to the baseline volume. Accordingly, the average of the baseline blocks was subtracted from each postfeeding block. Blocks of different diets were then compared with an ANOVA by use of a computer software program. Results between meals, with and without devazepide treatment, were also compared within the same diet. For the high-CHO diet, results obtained with the diluents only were also included in the comparison. Significance was set at a value of P < 0.05.

Gastric emptying analysis—All samples containing <0.3% CO2 were rejected to minimize analytic inaccuracies. The 13C:12C ratio of each breath sample was determined by automated continuous flow isotope ratio mass spectrometry and expressed relative to an international standard. This rate was converted to parts per million excess 13C, after subtraction of the mean value of 13C-abundance of the 3 baseline breath samples. The percentage dose recovery per hour of the administered isotope in the breath was calculated and plotted against time with the formula elaborated by Ghoos et al. The following parameters of gastric emptying were calculated from this curve: the gastric emptying coefficient, which reflects the gradient of the emptying curve and is a universal index of gastric emptying rate, was calculated according to Maes; t½, equivalent to the time at which the area under fitted cumulative 13C excretion curve demonstrates recovery of half the administered isotopic dose; and tmax. Curve fitting and calculation of constants were performed by least squares nonlinear regression analysis by use of a computer software program. The modeling techniques are described in detail by Sutton et al. Comparison of parameters of gastric emptying (ie, gastric emptying coefficient, t½, and tmax) between diets was determined by a Friedman 2-way ANOVA test for nonparametric analysis. All results are reported as mean ± SEM. Significance was set at a value of P < 0.05.

Results
Plasma CCK-like activity—All samples were extracted and assayed in duplicate. The standard curve ranged from 0 to 25 pmol/L (Figure 1). The sensitivity
of the assay, given by the commercial kit, was 0.3 pmol/L. Cholecystokinin concentrations of the RIA controls (low-dose and high-dose controls) were detected within the limits given by the kit. Standard CCK controls for the extraction procedure provided a 73.9% recovery.

For the recovery control, plasma samples obtained from a horse after an overnight of food deprivation were spiked with known concentrations of CCK-8 standard (0, 0.78, 1.36, 3.12, 6.25, 12.5, and 25 pmol/L) provided by the commercial kit (Figure 1). Recovery was good for all the concentrations (mean, 69%; range, 68% to 96%), except for the sample with 3.12 pmol/L (32% recovery). Plasma samples from horses that were fed either the high-fat or the high-CHO pelleted diet were also included in the assay. Cholecystokinin was not detected in any of the samples, including those that were treated with aprotinin.

Because CCK may be susceptible to degradation if plasma is not processed and frozen within 2 hours after collection, an additional experiment was performed to test whether early degradation of equine CCK was responsible for the failure of the RIA to detect CCK. After overnight food deprivation, a horse was offered a sweet feed meal (0.5 g/kg) mixed with 30 mL of corn oil. Blood samples were collected from the jugular vein before and 10, 20, 30, and 50 minutes after ingestion of the meal. Blood samples were centrifuged immediately after collection and the plasma frozen at –20°C for subsequent RIA. Because the aim of the experiment was to detect CCK and not to measure it, the samples were assayed in combination with only 2 RIA controls of CCK-8 standard (0 and 6.25 pmol/L) and 2 recovery controls with known original concentrations. Cholecystokinin was detected in the RIA and recovery controls, but not in the equine plasma samples. Finally, the bioassay also failed to detect CCK bioactivity in plasma samples from the horse given the high-fat meal that contained phenylalanine.

Effect of CCK-1 receptor blockade on intragastric bag volume—Intravenous administration of devazepide or the vehicle alone was associated with a rapid increase in barostat bag volume, indicating proximal gastric relaxation, which peaked by 3 minutes after injection and was followed by a steep decrease until it returned to baseline volume. We presume that the DMSO in the vehicle caused this response. Therefore, for this set of experiments, the period of baseline recording (30 minutes) was divided into 2 periods as follows: the first 20 minutes of recording, and the next 10-minute period that encompassed the postinjection relaxation. The mean bag volume of the latter period was significantly (P < 0.001 and P = 0.046 for the high-CHO meal with devazepide and high-fat meal with devazepide studies, respectively; and P = 0.008 for the high-CHO meal with vehicle studies) greater than that of the first 20-minute period. For this reason, the first 20 minutes comprised the baseline period used for data analysis for this set of experiments. On the other hand, no significant changes in bag volume were observed during the baseline period for the remaining experiments (those without treatment), and therefore, the entire baseline period (30 minutes) was used for their analysis.

Bag volume began to increase rapidly after initiation of ingestion of any meal (Figure 2), reached a peak volume, and then decreased gradually by the end of ingestion. Intragastric bag volume remained significantly greater than baseline volume for the entire postprandial period. Each postprandial volume represents values from which the baseline volume has been subtracted. *Significant (P < 0.05) difference between pairs of blocks at the same postprandial time.
prandial phase of the high-CHO and the high-fat meal (90 minutes), except for some discrete periods after the high-fat meal (by 1 hour after ingestion), where bag volume was not significantly different from baseline. A similar postprandial response was observed when horses were previously treated with devazepide or the vehicle. No significant difference was observed in the magnitude of response between experiments with and without pretreatment, except for the high-fat meal, where pretreatment with devazepide resulted in a significantly greater bag volume at 36, 44, 48 to 56, and 90 minutes after ingestion of the meal.

Effect of CCK-1 receptor blockade on gastric emptying—Treatment with devazepide before ingestion of the high-fat or the high-CHO meal resulted in a higher and more exponential peak for isotope recovery, compared with no treatment (Figure 3). Gastric emptying curves of the high-CHO meal with and without pretreatment with the vehicle were similar.

Devazepide treatment shortened the \( t_{1/2} \) and \( t_{\text{max}} \) of emptying of both meals, but only significantly with glucose enrichment (Table 1). For the high-fat meal, no significant difference was found between any of the gastric emptying indices.

\[ \text{Discussion} \]

The main objective of our study was to evaluate the effect of dietary fat and CHO on plasma CCK concentrations and of CCK-1 receptor blockade on accommodation of the proximal portion of the stomach and subsequent gastric emptying of high-fat and high-CHO meals. By use of a commercial nonspecific RIA, no plasma CCK-like activity was detected in the horses before and after ingestion of the high-fat and the high-CHO pelleted meals. Likewise, the bioassay technique failed to detect CCK activity of concentrated plasma obtained from a horse before and after ingestion of a sweet feed meal supplemented with corn oil and phenylalanine.

The failure to detect CCK-like activity in equine plasma samples may be explained by the inability of the technique to measure CCK. However, some reasons exist to question this possibility. First of all, it is known that CCK is well conserved among mammals and even nonmammalian vertebrates. Moreover, it is known that gastrin, which shares an identical C-terminal tetrapeptide sequence with CCK (minimal structure necessary for biological activity of both hormones), is highly conserved between horses and other mammals. Hence, it is reasonable to assume that the high structural

<table>
<thead>
<tr>
<th>Test meal</th>
<th>Mean ( t_{1/2} ) (h) ( \pm ) SEM</th>
<th>Mean ( t_{\text{max}} ) (h) ( \pm ) SEM</th>
<th>Mean GEC ( \pm ) SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-fat meal alone</td>
<td>2.28 ( \pm ) 0.18</td>
<td>1.81–2.85</td>
<td>1.63 ( \pm ) 0.08</td>
</tr>
<tr>
<td>High-fat meal + devazepide</td>
<td>1.71 ( \pm ) 0.21</td>
<td>1.31–2.39</td>
<td>1.22 ( \pm ) 0.22</td>
</tr>
<tr>
<td>High-CHO meal alone</td>
<td>2.67 ( \pm ) 0.38</td>
<td>1.77–3.75</td>
<td>1.96 ( \pm ) 0.26</td>
</tr>
<tr>
<td>High-CHO meal + devazepide</td>
<td>1.88 ( \pm ) 0.25*</td>
<td>1.11–2.41</td>
<td>1.35 ( \pm ) 0.20*</td>
</tr>
<tr>
<td>High-CHO meal + vehicle</td>
<td>2.69 ( \pm ) 0.16</td>
<td>2.26–3.25</td>
<td>1.90 ( \pm ) 0.16</td>
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*Significantly \( (P < 0.05) \) different from high-CHO meal alone.
homology of CCK is also maintained in horses and that the antibody of the commercial kit for human CCK used in our study, which binds the C-terminal sulphated octapeptide, should have the capacity to bind equine CCK. Second, a rabbit antibody against sulphated CCK-8, with the same sequence as the one used in our study, has been successful in detecting CCK in neuroendocrine cells of equine urethra. Finally, the bioassay also failed to detect CCK bioactivity in equine plasma samples that were concentrated prior to bioassay to increase the likelihood of detecting low CCK concentrations. Although plasma samples from only one horse were used for this technique, they were collected after the horse had ingested a mixed meal containing corn oil and phenylalanine, which are known to be potent stimulants of plasma CCK release in other species. We can only conclude from this that little, if any, CCK is released into the equine bloodstream under normal conditions.

Many studies have evaluated the effect of dietary fat—whether ingested, delivered into the stomach, or infused into the duodenum—on plasma CCK concentration. Fat stimulates release of CCK into the circulation in humans, rats, dogs, pigs, cats, cows, and chicks. Because dietary fat is invariably a potent stimulus of CCK release in all the above-mentioned species, it is surprising that in our study, postprandial plasma CCK was not detected after ingestion of the high-fat pelleted diet, especially because CCK-BIR cells have been found in equine duodenal tissue. In all species except pigs, CHO have been found to be, at best, weak stimulants of CCK release, compared with fat and protein. Starch or glucose is ineffective in increasing plasma CCK concentrations in rats and cats, whereas in humans, they have a weak to nonsignificant effect. Thus, in this respect, horses appear to be similar to other species.

Although we cannot totally exclude a failure of the RIA technique to detect CCK in plasma, the idea of a physiologic role for this peptide is supported by the results of our investigation of the effects of CCK-1 receptor blockade. Treatment with devazepide, a highly selective and potent antagonist, accelerated the gastric emptying of the glucose- and oil-enriched meals, but only significantly with the glucose enrichment. Acceleration of gastric emptying of a meal by CCK-1 receptor antagonists has been shown in other species, as well. However, this effect has been observed not only with CHOs but also with fat. Therefore, in contrast to other species, the regulatory functions of CCK on gastric emptying in horses may be more related to dietary CHO than fat content.

On the other hand, preprandial treatment with devazepide resulted in a significantly greater decrease in gastric tone at some time intervals after ingestion of the high-fat meal. This result is opposite to our expectations, as CCK-1 blockade abolishes the meal-induced decrease of gastric tone in other species. Although exogenous CCK can directly stimulate gastric smooth muscle contraction, this effect may be more experimental than physiologic, and the vagovagal-mediated relaxation effect of CCK seems to be more important than its direct effect on the smooth muscle. On the basis of our results, it is unlikely that CCK regulates the nutrient-induced feedback inhibition of gastric emptying by changes in proximal gastric tone. Instead, its effect may be mediated by modulation of antral or pyloric contractions.

The effect of devazepide treatment supports a role for CCK in modulation of gastric emptying in horses. That this occurred even though no plasma CCK activity could be measured is consistent with the current hypothesis that CCK functions in a paracrine fashion such that its release from gastrointestinal tract enteroendocrine cells in response to intraluminal nutrients is not necessarily reflected by increased plasma concentrations. Results of anatomic and functional studies in other species support this view. For example, nerve endings within the small intestinal mucosa are a likely target of CCK action because of their close proximity to enteroendocrine cells. Vagal sensory neurons are directly responsive to CCK, specifically through the CCK-1 receptor subtype. Results of inhibition of CCK-1 receptors with selective antagonists and selective destruction of vagal afferent c-fibers with the sensory neurotoxin capsaicin indicate that CCK mediates its effect, in part, in a neurally dependent fashion. The effect of CCK-1 antagonists is not only limited to nutrients that increase circulating concentrations of the peptide. For instance, ingestion and intestinal perfusion of CHOs, which do not increase plasma concentrations of CCK, inhibit gastric emptying via CCK-1 receptors, supporting the concept of a paracrine action. To summarize all these observations, Raybould and Lloyd proposed that CCK might be released by nutrients and achieve locally high concentrations that stimulate CCK receptors on afferent nerve endings within the duodenal mucosa.

In conclusion, in comparison to other species, horses are unique in that no measurable CCK is detected in their plasma in either the pre- or postprandial states. However, our results suggest that a role may exist for CCK in the regulation of the gastric motor response to a meal in horses and that, in contrast to other species, it may be more responsive to CHO than to fat. A vagovagal reflex most likely mediates this regulation, with CCK functioning as a paracrine intermediary at the intestinal level.
uid gastric emptying.

CCK antagonist.


References


