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European Journal of Pharmacology 273 (1995) 161–165

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Inhibition of food passage by omeprazole in the chicken

Remedios T. Mabayo, Mitsuhiro Furuse *, Jun-ichi Okumura

Laboratory of Animal Nutrition, School of Agriculture, Nagoya University, Nagoya 464-01, Japan

Received 31 August 1994; accepted 4 November 1994

Abstract

The effect of omeprazole, a proton pump inhibitor, on the forward passage of the crop contents of chicks receiving 20% medium chain or long chain triacylglycerol was studied. Medium chain triacylglycerol significantly delayed the crop emptying of chicks compared with long chain triacylglycerol. Omeprazole also significantly inhibited passage from the crop of the long chain triacylglycerol meal. Application of omeprazole induces achlorhydria and consequently hypergastrinemia but chicken gastrin lower than 100 nmol/kg did not delay crop emptying. The addition of hydrochloric acid (HCl) to the diet reversed the action of omeprazole on the crop emptying of chicks. We conclude, then, that omeprazole delayed the crop emptying in chicks as a consequence of inhibition of acid secretion, although the mediator is not gastrin.

Keywords: Omeprazole; Crop emptying; Medium chain triacylglycerol; Long chain triacylglycerol; Acid; (Chick)

1. Introduction

Medium chain triacylglycerol reduced food intake in chicks (Furuse et al., 1992), in part by delaying crop emptying (Mabayo et al., 1992). The mechanisms controlling the crop emptying in chicks are poorly understood. Recently, Martinez et al. (1993a) reported that cholecystokinin (CCK) and chicken gastrin inhibited gastroduodenal motility in the chicken. Although it was reported that medium chain triacylglycerol enhanced the release of CCK in rats (Douglas et al., 1990) and chicks (Mabayo et al., 1992), CCK-receptor antagonists failed to inhibit the satiety effect of medium chain triacylglycerol (Furuse et al., 1993a) and to antagonize CCK actions (Martinez et al., 1993a) in chickens. Furuse et al. (1993b) reported that medium chain triacylglycerol greatly enhanced the release of chicken gastrin. Omeprazole, a drug which inhibits acid secretion, was shown to increase chicken gastrin secretion in chicks (Campbell et al., 1991; Furuse et al., 1993b) and decreased gastric emptying in rats (Larsson et al., 1985). Intragastric instillation of 50 mM hydrochloric acid (HCl) inhibited gastric emptying in rats (Forster et al., 1990). These observations support the hypothesis that chicken gastrin release by medium chain triacylglycerol is responsible for the delayed crop emptying. In this study, therefore, we examined whether or not the inhibition of acid secretion and the increased release of chicken gastrin affected crop emptying of chicks fed dietary medium chain triacylglycerol or long chain triacylglycerol.

2. Materials and methods

2.1. General

Day-old Single Comb White Leghorn male chicks (Hattori Hatchery, Nagoya, Japan) were housed in wire-meshed cages in a constant temperature (30°C) room. They received a commercial chick mash (Marubeni Shiryo Co., Tokyo, Japan) until they were selected for each experiment. Before the start of each experiment, the chicks were fasted overnight (about 14 h) with free access to water.

In each experiment the birds received a single experimental meal (Table 1). Corn oil (Wako Pure Chemical Industries, Osaka, Japan) and glyceryl caprylate were used as long chain and medium chain triacylglycerol sources, respectively. The medium chain triacylglycerol source in this study was donated by Kao

* Corresponding author. Tel. (052) 789-4077, fax (052) 789-4012, telex 442 2120 ANUNAG J.

SSDI 0014-2999(94)00684-9

Table 1
Composition of experimental diets (g/kg)

Ingredient	MCT [a]	LCT [a]
Isolated soybean protein	226	
Mineral mixture [b]	58.8	
Vitamin mixture [c]	2	
Choline chloride	1.5	
Inositol	1	
L-Methionine	2.9	
L-Threonine	1.2	
Glycine	4.2	
Cellulose	100	
Corn starch	402.4	
Corn oil	20	200
Coconado RK [d]	180	0

[a] MCT, medium chain triacylglycerol; LCT, long chain triacylglycerol. [b] Contained 20.7 g $CaHPO_4 \cdot 2H_2O$, 14.8 g $CaCO_3$, 10 g K_2HPO_4, 3 g KCl, 6 g NaCl, 3 g $MgSO_4$, 0.5 g $FeSO_4 \cdot 7H_2O$, 0.35 g $MnSO_4 \cdot 5H_2O$, 2.6 mg KI, 40 mg $CuSO_4 \cdot 5H_2O$, 62 mg ZnO, 1.7 mg $Na_2MoO_4 \cdot 2H_2O$, 0.4 mg Na_2SeO_3, 0.93 mg $CoCl_2$. [c] Contained 15 mg calcium pantothenate, 6 mg riboflavin, 4 mg pyridoxine hydrochloride, 40 mg nicotinic acid, 1.5 mg folic acid, 0.2 mg biotin, 0.02 mg cyanocobalamin, 3 mg thiamin hydrochloride, 200 ICU vitamin D_3, 0.5 mg vitamin K^3, and 1.93 g glucose. The DL-α-tocopheryl acetate (10 IU) and retinyl acetate (1700 IU) were dissolved in corn oil. [d] Coconado RK, glyceryl tricaprylate (donated by Kao Corp., Wakayama, Japan).

Corporation, Wakayama, Japan. The medium chain triacylglycerol diet was supplemented with 20 g corn oil/kg to meet the requirement for essential fatty acids. The test meals were blended with water except in the HCl study (section 2.4) and tube-fed through the esophagus into the crop. The amount of slurry intubated was adjusted according to the age and body weight of the birds.

2.2. Effects of omeprazole on crop emptying rate

The birds (21 days old) were fasted for 3 h, were selected and distributed into 4 groups of 7 birds. Omeprazole was suspended in 0.25% (w/v) methyl cellulose solution and administered by gavage 15 h before the experiment (400 μmol/kg body weight). During the experiment the birds were intubated with 7 ml slurry containing 2.85 g medium chain or long chain triacylglycerol diet. Crop emptying was examined 3 h after intubation.

2.3. Effects of chicken gastrin on crop emptying rate

To find out whether or not gastrin might mimic the action of omeprazole, fasted birds (15–16 days old) received (i.p.) 10 pmol, 100 pmol or 1 nmol chicken gastrin/kg body weight or saline as vehicle, prior to diet intubation. The birds were then intubated with 6 ml slurry containing 2.40 g medium chain or long chain triacylglycerol diet. Crop emptying was examined 3 h after intubation. In a further experiment, birds received (i.p.) 1 nmol chicken gastrin/kg body weight or saline, followed by 6 ml slurry containing 2.50 g long chain triacylglycerol diet. Only the long chain triacylglycerol diet was used since omeprazole drastically delayed the crop emptying of chicks intubated with the long chain triacylglycerol diet. Crop emptying was examined 1 or 2 h after intubation. Furthermore, birds received (i.p.) 10 or 100 nmol chicken gastrin/kg body weight or saline followed by 6 ml slurry containing 2.48 g long chain triacylglycerol diet and crop emptying was examined 2 h after intubation.

2.4. Effects of HCl on crop emptying rate

The possibility that the inhibition of acid secretion by omeprazole caused the delayed diet passage from the crop was tested in birds (17 days old) fasted for 3 h and receiving omeprazole or vehicle 15 h before the experiment. During the experiment the birds were intubated with 6 ml slurry containing 0.45% saline or 75 mM HCl and 2.50 g long chain triacylglycerol diet. Crop emptying was examined 3 h after intubation.

2.5. Determination of crop emptying rate

Crop emptying was examined by incision of the skin of the crop and clamping the lower and upper crop junctions under light anesthesia with diethyl ether. The crop was then cut distal to the clamps, and crop content was removed and dried at 55°C for 24 h and weighed. Crop emptying rate was assessed by measuring the dry weight of a meal remaining in the crop and expressed as the relative weight of the crop content to the amount of food intubated.

2.6. Statistics

The data in all experiments, except HCl effect and gastrin injection at 10 or 100 nmol/kg body weight, were subjected to two-way analysis of variance (fat source × treatment) and significance of difference between means was determined by t-test. One-way analysis of variance was applied to the HCl effect study and gastrin injection at 10 or 100 nmol/kg and significance of difference was assessed by Duncan's multiple range test. All of the data analyses were done using a commercially available statistical package (SAS, 1985). Values are presented as means ± S.E.M. Statistical significance was assumed at $P < 0.05$.

3. Results

Fig. 1 shows the relative crop content of chicks administered omeprazole (400 μmol/kg body weight)

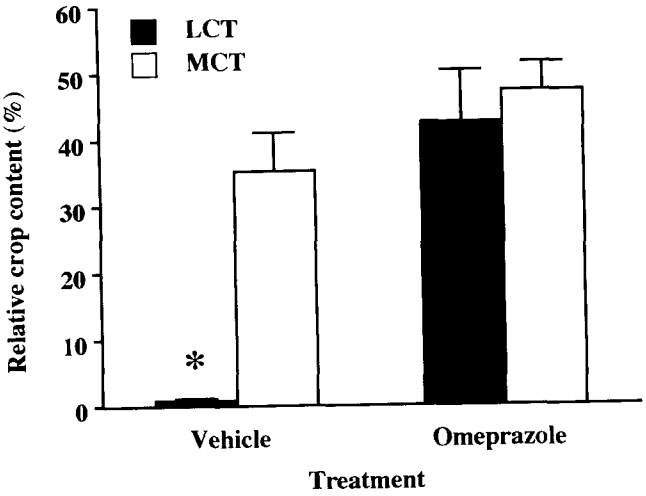

Fig. 1. Relative crop content of chicks (22 days old) administered with omeprazole (400 μmol/kg body weight) 15 h before the experiment. During the experiment the chicks were intubated with 7 ml slurry containing 2.85 g diet with 20% medium (MCT) or long chain triacylglycerol (LCT) and crop emptying was done after 3 h. Values are means of 7 birds ± S.E.M. * Significant difference between MCT and LCT administered with vehicle and between vehicle- and omeprazole-administered LCT groups at $P < 0.001$.

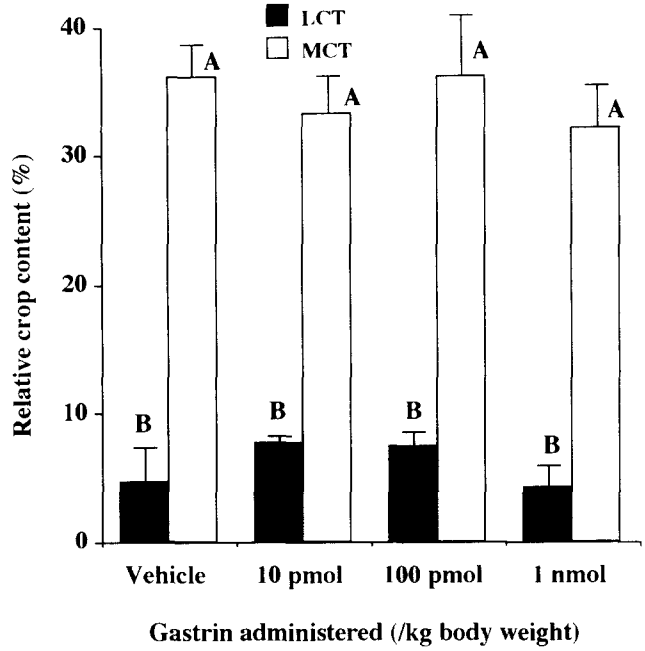

Fig. 2. Relative crop content of chicks (15–16 days old) injected (i.p.) with gastrin at different doses or vehicle and intubated with 6 ml slurry containing 2.40 g diet with 20% medium (MCT) or long chain triacylglycerol (LCT). Crop emptying was done at 3 h after intubation. Values are means of 7 birds ± S.E.M. ^{AB}Significant difference between MCT and LCT within the same treatment at $P < 0.001$.

or vehicle by gavage 15 h before the experiment. The crop was emptied at 3 h after receiving medium chain triacylglycerol or long chain triacylglycerol. Medium chain triacylglycerol significantly delayed the crop emptying of chicks compared with long chain triacylglycerol without omeprazole. Omeprazole significantly delayed the crop emptying of chicks given long chain triacylglycerol diet.

Fig. 2 shows relative crop content of chicks injected (i.p.) with 10 pmol, 100 pmol or 1 nmol chicken gastrin/kg body weight or saline as vehicle prior to intubation of dietary medium chain triacylglycerol or long chain triacylglycerol. The crop was emptied at 3 h after diet intubation. Medium chain triacylglycerol delayed crop emptying of the chicks compared with long chain triacylglycerol. There was no significant difference between any dose at which chicken gastrin was injected.

Fig. 3 shows the relative crop contents of chicks injected (i.p.) with 1 nmol chicken gastrin/kg body weight or saline as vehicle prior to intubation of dietary medium chain triacylglycerol or long chain triacylglycerol. There was no significant difference between treatments, although there was a significant difference with time.

Fig. 4 shows relative crop content of chicks injected (i.p.) with 10 nmol, 100 nmol chicken gastrin/kg body weight or saline as vehicle prior to intubation of dietary long chain triacylglycerol. The crop was emptied at 2 h after diet intubation. Diet passage from the crop was significantly delayed by injection of 100 nmol chicken gastrin/kg body weight.

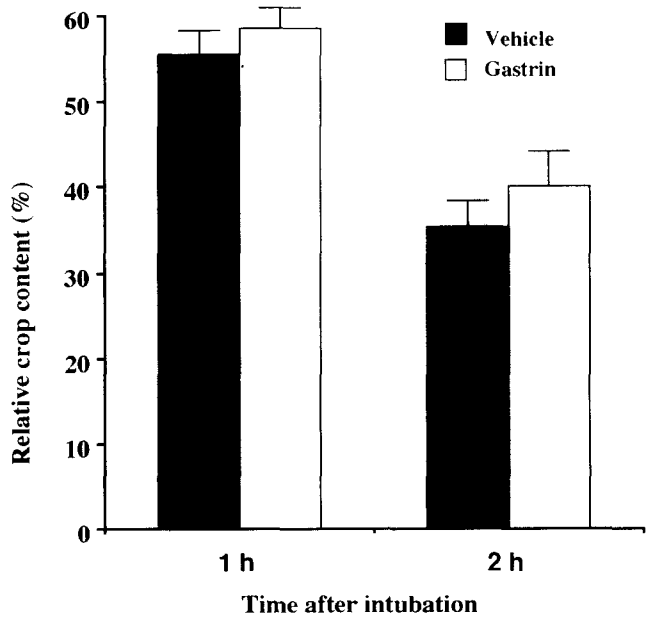

Fig. 3. Relative crop content of chicks (15 days old) injected (i.p.) with gastrin (1 nmol/kg body weight) or vehicle and intubated with 6 ml slurry containing 2.50 g diet with 20% long chain triacylglycerol (LCT). Crop emptying was done at 1 or 2 h after intubation. Values are means of 7 birds ± S.E.M. Relative crop contents were significantly different between 1 and 2 h at $P < 0.001$.

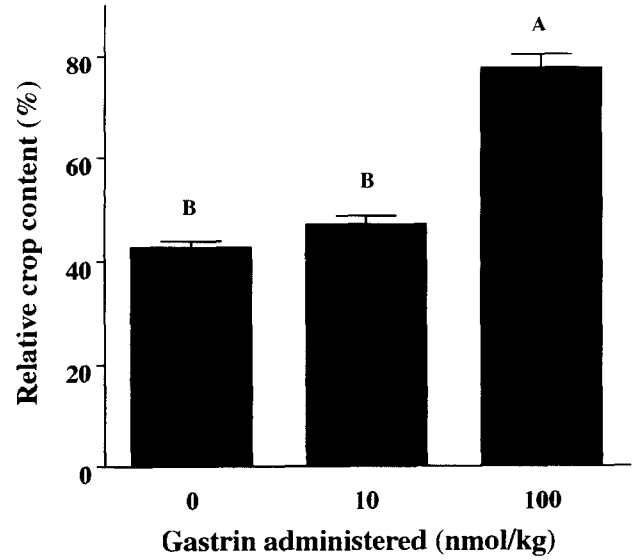

Fig. 4. Relative crop content of chicks (15 days old) injected (i.p.) with gastrin (10 or 100 nmol/kg body weight) or vehicle (0) and intubated with 6 ml slurry containing 2.48 g diet with 20% long chain triacylglycerol (LCT). Crop emptying was done 2 h after intubation. Values are means of 7 birds ± S.E.M. ^{AB}Significantly different at $P < 0.001$.

Fig. 5 shows the relative crop content of chicks receiving omeprazole (400 μmol/kg body weight) or vehicle by gavage 15 h before the experiment. The birds then received long chain triacylglycerol diet with either saline or HCl. Omeprazole significantly delayed crop emptying. The addition of HCl to the test meal significantly enhanced the crop emptying rate.

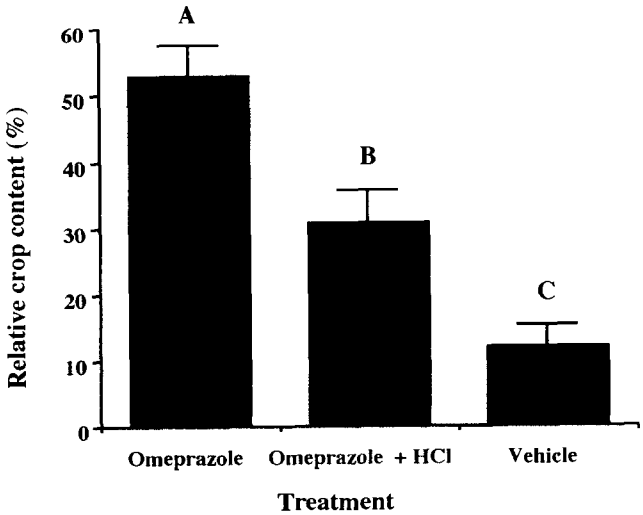

Fig. 5. Relative crop content of chicks (18 days old) administered with omeprazole (400 μmol/kg body weight) 15 h before the experiment. During the experiment the chicks were intubated with 6 ml slurry containing 0.45% saline or 75 mM HCl and 2.50 g diet with 20% long chain triacylglycerol (LCT); crop emptying was done after 3 h. Values are means of 7–9 birds ± S.E.M. ^{ABC}Significantly different at $P < 0.05$.

4. Discussion

The present series of experiments were done to examine the factor regulating crop emptying in chicks fed a medium chain triacylglycerol diet. Medium chain triacylglycerol greatly enhanced the release of chicken gastrin (Furuse et al., 1993b). When plasma chicken gastrin was enhanced by omeprazole, the difference in crop emptying between medium chain triacylglycerol and long chain triacylglycerol disappeared (Fig. 1). This result led us to investigate two possibilities: (i) the effect of gastrin and (ii) the effect of acid inhibition, because omeprazole induces achlorhydria and hypergastrinemia (Dockray et al., 1993). Omeprazole was reported to reduce food intake in chicks (Campbell et al., 1991) and in the same study the reduction of food intake was reversed by administering a gastrin receptor antagonist. In this study, however, the i.p. injection of gastrin at certain doses did not mimic the action of omeprazole on the crop emptying of chicks given medium chain triacylglycerol or long chain triacylglycerol diet even at pharmacological doses, but at 100 nmol/kg. Omeprazole induced the release of gastrin at concentrations ranging from 1340 to 1763 pM in chickens (Furuse and Dockray, unpublished data). The effect of chicken gastrin on the gastroduodenal motility in the chicken was investigated in a different study and it was reported that motility was inhibited but only at a pharmacological dose; lower doses of chicken gastrin had no effect on gastric motility in the chicken (Martinez et al., 1993a). To verify whether or not the duration of action of gastrin was shorter than 3 h, the crop was emptied at 1 or 2 h after diet intubation. There was no effect of gastrin over these periods but an effect was prevalent at 2 h after intubation with 100 nmol/kg, which was an excessively high dose.

The digestive tract of the fowl has distinct properties compared to other species. In chickens the proventriculus secretes the acid and the gizzard is a muscular grinding organ, analogous to the mammalian antrum. Crop emptying might be expected to be coordinated with functions in other parts of the gastro-intestinal tract. There are reports that CCK is the major factor controlling gastrointestinal motility in chickens (Savory et al., 1981; Martinez et al., 1993b). The doses administered in these studies, however, were supra-physiological and other factors are likely to be important when CCK levels are physiological. Vergara et al. (1989) reported that the rate of emptying of the crop was not dependent on the markers, regardless of their size or state, indicating that the crop does not selectively empty different foods. This statement could not be applied to chicks fed diets containing medium chain triacylglycerol or long chain triacylglycerol since diet passage from the crop was delayed by dietary medium chain triacylglycerol. There are unidentified factors causing

the delayed crop emptying with dietary medium chain triacylglycerol in which the crop may not play a major role.

The delay in crop emptying caused by omeprazole seems not to be due to the release of gastrin, suggesting inhibition of acid can be a contributing factior. HCl helps in the breakdown of connective tissue and muscle fibers, activates pepsins and provides a medium of low pH in which pepsins can act (Sanford, 1992). In rats, intragastric instillation of 50 mM HCl inhibited gastric emptying (Forster et al., 1990) and this result was obtained in rats in which acid secretion was normal. Omeprazole, in the dose used, completely inhibits HCl secretion, consequently, it increased gastric and duodenal pH in healthy humans (Rubinstein and Hojgaard, 1993). HCl induced lowering of intracellular pH in rabbits (Tobey et al., 1993). Plasma gastrin was increased by omeprazole and was decreased by gastric instillation of 75 mM HCl in rats (Dockray et al., 1993). In this study, the addition of HCl enhanced crop emptying in achlorhydric chickens which should have mimicked the role of the proventriculus. HCl may stimulate the crop emptying at physiological conditions. Gastric chymes are emptied rapidly at pH 7 (Kelly, 1981) but the greater the concentration of an acid, the slower the gastric emptying was (Hunt and Knox, 1972). The proventriculus, then, being the acid producing portion in the digestive tract of the chicken, had a major influence on the rate of crop emptying of the diet. It is concluded that the delayed crop emptying induced by omeprazole was caused by achlorhydria. However, the highest level of gastrin administered (100 nmol/kg) delayed the crop emptying which may imply the need to use a gastrin receptor antagonist for further clarification. Moreover, further studies are needed to identify the major factors controlling crop emptying of dietary medium chain triacylglycerol.

Acknowledgements

The authors are very grateful to Prof. G.J. Dockray of the University of Liverpool, UK for critical reading of the manuscript. This study was supported by a grant-in-aid (06660352) for scientific research from the Ministry of Education, Science and Culture, Japan.

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