The Relationship between Gastrointestinal Transit and Motility in Dogs with Postoperative Ileus

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We investigated the relationship between gastrointestinal (GI) transit and motility during postoperative ileus in dogs undergoing a single laparotomy. We combined X-ray radiography for a GI transit study with chronically implanted force transducers (FTs) for a GI motility study. Radio-opaque markers made of polyethylene and steel wires or barium sulfate were used to examine solid substance transit or liquid substance transit. For a while after the end of the operation, postoperative ileus was observed, with weak irregular contractions of the GI tract. Transmission of the contractions to the lower GI tract was then observed. The start point of interdigestive migrating contraction (IMC)-like motility was observed in the order of small intestine (I-IMC), duodenum (D-IMC), and stomach (G-IMC), and IMC proceeded gradually after the operation. The gastric emptying time of a solid marker was 73.6 ± 2.3 h ($n=5$), and depended on the time of first occurrence of G-IMC ($r=0.674$, $p=0.006$). The gastric emptying of the liquid marker was finished before the time of the first occurrence of G-IMC, and its small intestinal transit time correlated with the time of the first occurrence of G-IMC ($r=0.888$, $p=0.018$). Using combined X-ray radiography and FTs we found that recovery from postoperative ileus was aided by GI motility in which contractions were transmitted from the stomach to the lower GI tract, like IMC.

Key words gastrointestinal transit; gastrointestinal motility; postoperative ileus; interdigestive migrating contraction; radiography

Disorders of gastrointestinal (GI) motility are generally present after laparotomy, with several days required for recovery.¹⁾ Laparotomy is performed during fasting because it leads to postoperative ileus in the early period after the operation. Interdigestive GI motility, *i.e.*, interdigestive migrating contraction (IMC), is therefore observed on recovery. The motor activity of the GI tract in the process of recovery from postoperative ileus has been experimentally confirmed in dogs by the measurement of GI motility using chronically implanted force transducers (FTs).²⁾ There are other methods for the measurement of GI motility in dogs, *i.e.*, use of a balloon catheter and electromyography.^{3,4)} We can directly observe contractions of the circular muscle of the GI tract and the propagation of these contractions using FTs.⁵⁾ GI transit such as gastric emptying and small or large intestinal transit have been measured in dogs by many methods. These include drug absorption of acetaminophen (AAP), salicylsulfapyridine (SSP) and tolafenamic acid (TA),^{6–8)} scintigraphic measurement of radioactivity of technetium-99m (^{99m}Tc), indium-111 (¹¹¹In), or cobalt-57 (⁵⁷Co),^{9,10)} and X-ray radiography of radio-opaque markers.^{11,12)} However, no simultaneous investigation of both GI motility and GI transit during postoperative ileus and recovery has been performed in a dog model.

Clinically, ileus after laparotomy is a major impediment to patient recovery, since it necessitates the use of a nasal tube for the drainage of retained intragastric fluid and parenteral alimentation.¹⁾ Therefore, attempts have been made to reduce the duration of postoperative ileus, to permit removal of the nasal gastric tube as early as possible, and to enable oral nutritional intake. It is thought that food residua and secretions remaining in the GI tract during ileus cause abdominal distention and disorders.

Normal GI motility is roughly classified into two types. One is the contractile motility of smooth muscle in the interdigestive state, while the other is contractile motility contin-

ued for a long period of time in the postprandial state. Interdigestive GI motility has 4 phases: phase I (silent state), phase II (random irregular contractions), phase III (frequent regular contractions) and phase IV (rapid decrease in incidence and intensity after phase III).¹³⁾ Phase III begins from the stomach and duodenum, and is propagated to the lower GI tract. This motility is called IMC, and it is thought that IMC plays the role of housekeeper by inducing the transit of gastric juice, food residua and exfoliated epidermis of the mucous membrane in the GI tract.¹⁴⁾ The IMC is observed in the interdigestive state, so it is thought the IMC is finally recognized as GI motility in recovery after laparotomy. However, it is unclear whether the time of appearance of IMC-like motility corresponds to the recovery time of GI transit ability.

In this study, we simultaneously investigated the relationship between GI transit and motility during postoperative ileus with that after recovery from ileus in dogs using X-ray radiography and chronically implanted FTs to clarify the above hypothesis.

MATERIALS AND METHODS

Laparotomy A total of 16 healthy male beagle dogs (OBC, Shizuoka, Japan) weighing 9–12 kg were used. The animals were housed in an air-conditioned room at 22 °C and a 12 h light cycle, fed standard laboratory diet (Canine Diet #4360, Purina Japan, Tokyo, Japan) and given water *ad libitum*. The animals were fasted for 24 h before surgery (*ad libitum* intake of water was permitted) and anesthetized with sodium pentobarbital (Nembutal®, Dainabot, Osaka, Japan), 35 mg/kg, *i.v.*, and the laparotomy was performed by an aseptic procedure. The external jugular vein was catheterized (ANTHRON®, Toray Medical, Tokyo, Japan) for drug administration. Then, 1 mg atropine sulfate was administered through the catheter, and FTs (F-12IS, Star Medical, Tokyo,

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Japan) were sutured with a silk thread to the serosal surface of the antrum of the stomach (15 cm orally from the pylorus), duodenum (15 cm anally from the pylorus), jejunum (3 points at 70, 170, and 220 cm anally in the entire length of 300 cm from the ligament of Treitz to the ileocecum), and colon (15 cm anally from ileocecum) to record the contractile activities of the annular muscle. The leads from FTs were passed under the skin to an incision between the bilateral scapular region, where they were brought out of the body and fixed. It took about 3 h from the start of the operation to the end. Postoperatively, a jacket was placed on the dog for protection of the leads and catheter, and 1 g of ceftriaxone sodium (Rocephin[®], Japan Rosch, Tokyo, Japan) was locally administered at the surgical wound at the closing of the laparotomy to prevent infection. In addition, 500 ml of KN[®] (Otsuka Pharmaceutical, Tokushima, Japan) fluid in which 0.5 g of ceftriaxone sodium was dissolved and infused at a rate of 500 ml/d. The dogs were given no food or water during the recording of GI motility.

Measurement of GI Transit and Motility GI motility was recorded with a personal computer (PC-9801, NEC, Tokyo, Japan) continuously for 99 h after the operation using an organ motility analysis system (ESC-820, Star Medical, Tokyo, Japan) under the condition of consciousness and no restriction. The three solid radio-opaque markers and 5 ml barium sulfate (75%, w/v) as a solid substance for contrast medium or 20 ml barium sulfate (75%, w/v) as a liquid substance were administered into the stomach through the gastric tube just before the end of the operation. Abdominal X-rays were taken 4 times daily using X-irradiation equipment (CMB80 special type, SOFTEX, Tokyo, Japan; 80 KVP, 20 mA, 0.5 s) under inhalation anesthesia with nitrous oxide-oxygen-fluothane (GOF) gas at 0830, 1200, 1630 and 2000 h. The solid radio-opaque marker was made of enclosed wires in a low-density polyethylene tube with a diameter 6 mm, 14 mm long, and 400 mg in weight, and a specific gravity of about 1.^{12,15,16} The GI tract was divided into the stomach, small intestine, colon, and rectum based on the anatomical position in abdominal X-rays. Using the above division, a score was determined for the position of solid radio-opaque marker or the top and end of barium sulfate.¹⁶ The geometric mean as an index of transit was calculated as the mean score of every measurement point. Gastric emptying

time was calculated as the mean time at which each score became 1. In the same fashion, the small intestinal transit time was calculated as the mean time at which each score became 2. When radio-opaque markers were not emptied from the stomach or passed through the small intestine until 99 h after the operation, gastric emptying time and small intestinal transit time were regarded as 99 h. The time of first occurrence of IMC-like contractions from the small intestine to the distal (I-IMC), from the duodenum to distal (D-IMC), and from the stomach to distal (G-IMC) were read from the measurement motility chart.

Statistical Analysis The correlations between the time of gastric emptying, small intestinal transit and the time of occurrence of I-IMC, D-IMC, and G-IMC were calculated. Results were expressed as the mean $\pm$ S.E.M. Statistical significance was determined by Student's *t*-test. *p* values of less than 0.05 were considered significant. Coefficients of correlation (*r*) and their *p* values were also determined.

RESULTS

Various conditions of measurement were examined using normal dogs with chronically implanted FTs. The effect of the volume of administration of barium sulfate on this model was investigated. Weak contractions continued in the stomach and duodenum when 30 ml of barium sulfate was administered interdigestively, but phase III contractions were not observed for 4 h. In this case, there was no effect of barium sulfate on lower GI motility (Fig. 1). The upper GI motility of IMC just after the administration of 20 ml of barium sulfate was affected, however the next IMC was normal GI motility (Fig. 2). The effect of GOF anesthesia on this model was also investigated. GOF anesthesia suppressed GI motility, especially in the upper part of the GI tract. However, the propagation of phase III contractions from the upper part to the lower part of the GI tract was not affected by anesthesia (Fig. 3).

Postoperative ileus was observed, and weak irregular contractions were observed in all parts of the GI tract for about 20 h after laparotomy in dogs. These weak contractions grew larger in amplitude, and collected in clusters 1–2 min in length for about 20–30 h after laparotomy. Next, giant contraction groups called phase III contractions were observed

Fig. 1. A Typical Chart of GI Motility after Administration of 30 ml of Barium Sulfate to a Normal Dog

GA, gastric antrum; D, duodenum; J1, jejunum-1; J2, jejunum-2; I, ileum; C, colon.

Fig. 2. A Typical Chart of GI Motility after Administration of 20 ml of Barium Sulfate to a Normal Dog

GA, gastric antrum; D, duodenum; J1, jejunum-1; J2, jejunum-2; I, ileum; C, colon.

Fig. 3. A Typical Chart of GI Motility in a Normal Dog Anesthetized GOF

GA, gastric antrum; D, duodenum; J1, jejunum-1; J2, jejunum-2; I, ileum; C, colon.

in the lower part of the GI tract, and then gradually in the upper part. These phase III contractions were propagated to the lower part of the GI tract as IMC-like motility, from about 30 h after laparotomy and thereafter. Finally, phase III contractions were observed in the stomach, and these were propagated to the lower part of the GI tract as IMC-like motility (Fig. 4). There was no difference between the liquid marker group or solid marker group in mean times of first occurrences of I-IMC, D-IMC and G-IMC (Table 1). On the other hand, the gastric emptying time and small intestinal transit time of the liquid marker were significantly shorter than those of the solid marker (Table 1). Diffusion of the liquid marker in the GI tract was observed, and the geometric mean value of the top of this marker was about 1 point higher than that of the end (Fig. 5). Transit of the solid marker from the stomach was not completed at 50 h after operation (Fig. 5). GI transit did not occur, due to the presence of only weak irregular motility, during the early postoperative period, but did occur with IMC-like motility. In particular, the gastric emptying time of the solid marker was correlated with the time of first occurrence of G-IMC (Fig. 6). The small intestine transit time of the liquid marker was correlated with the time of first occurrence of G-IMC (Fig. 7).

DISCUSSION

Several methods are available for the evaluation of GI transit, *i.e.*, drug absorption of AAP or SSP, scintigraphic measurement of radioactivity of a radioactive substance such as ^{99m}Tc, and X-ray radiography of radio-opaque substances such as barium sulfate. Of these methods, X-ray radiography is considered useful and is widely used in many facilities where radiographic equipment is available. This method can clearly detect GI transit with neither invasive procedures nor specific equipment. When taking X-rays of dogs, it is necessary to keep them anesthetized. However, anesthesia sedates the central nervous system and can decrease GI motility since it is under autonomic nerve system control.¹⁷⁾ To decrease this effect, we chose GOF anesthesia because of its rapid induction and emergence and its lack of metabolism in the body. Although this anesthesia suppressed GI motility, especially in the upper part of the GI tract, in healthy dogs it affected neither IMC during anesthesia nor IMC after emergence.

Alimentary content is transported by GI motility. Research using meals to examine GI transit have shown that liquid meal transit is faster than that of solid meals, and that the

Fig. 4. A Typical Chart of GI Motility on Dogs with Postoperative Ileus
GA, gastric antrum; D, duodenum; J1, jejunum-1; J2, jejunum-2; I, ileum; C, colon.

Fig. 5. GI Transit during Postoperative Ileus in Dogs Measured with Barium Sulfate and Solid Radio-opaque Marker
Each point represents the geometric mean of 6 dogs or 15 markers.

Table 1. Mean Values of Parameters for Postoperative Ileus in Dogs

	n	Mean time after laparotomy (h)				
		I-IMC	D-IMC	G-IMC	GE	IT
Barium sulfate	6	32.3±1.3	38.0±2.2	62.0±9.3	45.5±4.5***	54.3±4.7***
Solid marker	5	34.2±3.9	39.0±5.3	73.8±8.0	73.6±2.3	78.9±2.8

****p*<0.001: significantly different from the mean time of the barium sulfate group and solid marker group by Student's *t*-test. Results are expressed as means±S.E.M. I-IMC, D-IMC, G-IMC: the first times of occurrence of I-IMC, D-IMC, and G-IMC, respectively. GE, gastric emptying time; IT, small intestinal transit time.

Fig. 6. The Correlation between Gastric Emptying Time and the Time of First Occurrence of IMC-Like Motility during Postoperative Ileus in Dogs Measured with Solid Radio-opaque Marker (A) and Barium Sulfate (B)

Fig. 7. The Correlation between Small Intestinal Transit Time and the Time of First Occurrence of IMC-Like Motility during Postoperative Ileus in Dogs Measured with Solid Radio-opaque Marker (A) and Barium Sulfate (B)

lower the viscosity of a meal is, the faster the meal is transported.^{10,18)} The components of a meal can also affect transit; the fattier a meal is, the slower its transit.¹⁹⁾ Substances rich in fiber slow intestinal transit and encourage water secretion in the colon.²⁰⁾ pH in the intestine can also influence transit, since an alkaline condition in the duodenum stimulates the secretion of motilin.²¹⁾ Since a laparotomy is performed under fasting, a marker with calories, as regular meals have, would not be suitable for the evaluation of postoperative GI transit and motility. Presumably a substance which can be neither absorbed nor degraded would be preferable. Both barium sulfate and solid markers composed of polyethylene meet these conditions.

The contents of the stomach during postoperative ileus are secretions from the GI tract, old mucous membrane of the intestines and any food residue which has not been emptied during fasting. We therefore assumed that use of a liquid meal would be suitable for evaluation of GI transit and motility, and we employed a contrast medium of barium sulfate as a liquid meal. However, since its specific gravity is high, we assumed that barium sulfate can influence GI motility. We estimated that the administration of 30 ml of barium sulfate to fasting healthy dogs suppressed GI motility, but that administration of 20 ml affected it weakly. In this study, it was also confirmed that in healthy dogs gastric emptying was completely finished 3 h after the administration of barium sulfate and that barium sulfate moved to the colon at 6 h after administration. The administration of atropine suppressed GI motility, and an approximate 3 h delay in transit was observed compared with that of healthy dogs. The administra-

tion of atropine led to the diffusion of barium sulfate throughout the intestine (data not shown). We presumed that in a postoperative ileus model, more diffusion of barium sulfate would be observed and that the observation of transit would be required at both the front and the end of barium sulfate movement. We confirmed that in dogs with postoperative ileus, the transit of barium sulfate persisted for a long time, resulting in its diffusion in the intestine, and that there was a large difference in transit time between the front and the end of barium sulfate movement. In addition, even early in the postoperative period, when there was little gastric motility, transit from the stomach was observed. This appeared to be due to the pressure slope rather than GI motility. This finding appeared to suggest that the GI transit of barium sulfate is not always correlated with motility. Therefore, the results of the study using barium sulfate could not clearly explain the relationship between GI transit and motility.

We used solid markers to identify the relationship between GI transit and motility more clearly. In an experimental model of postoperative ileus, decisive GI motility during recovery is considered to be an occurrence of IMC, which is observed during fasting. We confirmed the finding that secretions increase in the stomach during postoperative ileus in dogs after single laparotomy (data not shown). This was accompanied by a lack of IMC-like motility during the period of GI paralysis. In order to examine the relationship between IMC-like motility and GI transit, evaluation of solid marker transport from the stomach by IMC is required. The speed of emptying solid substances from the stomach varies with the size of such substances. In dogs, the transit of substances of larger diameter is slower, and it has been reported that substances of a diameter of more than 5 mm move at almost the same speed as observed in healthy dogs.¹⁵⁾ Measurement of whole GI transit time with radio-opaque markers, which are used for solid substances, was established by Hinton *et al.* in 1969.²²⁾ In Japan, Satake *et al.* first reported this method in 1988.¹⁶⁾ Hinton *et al.* used disk-shaped hard markers with diameters of 2, 3 and 5 mm made of polyurethane board containing 20% barium sulfate. Satake *et al.* used a columnar marker 1 mm in diameter, 12 mm long and about 30 mg in weight made of barium sulfate and silicon rubber. In addition, the use of markers of various diameters, lengths and specific gravity has been reported.^{23,24)} Recently, many clinical studies using radio-opaque markers 2 mm in diameter in which barium sulfate is hardened with methylcellulose or SITZMARKS (4.5 mm diameter, 2 mm thick, KANSYL Pharmaceuticals, U.S.A.) have been performed.²⁵⁾ In the present study, we used a columnar radio-opaque marker 6 mm in diameter. A marker of this size should be transported through the pyloric valve by IMC. In fact, we confirmed that the gastric emptying time of a solid marker agreed with the time of the first occurrence of G-IMC. Regarding solid substances, transit from the stomach to the duodenum dominated, following GI transit times. Both liquid and solid markers were transported by IMC-like motility from the duodenum to the lower intestine. Regardless of the type of marker, transit time through the intestine was weakly correlated with G-IMC, but to a greater extent than with I-IMC and D-IMC. The occurrence of G-IMC appears to play an important role in GI transit. Yokoyama *et al.* reported that inducing gastric phase III activity in the early postoperative period lead to the recovery

of depressed GI motility after laparotomy.²⁾ Our findings support their results.

We investigated GI transit and motility, using radio-opaque markers and FTs, respectively, in dogs with postoperative ileus after single laparotomy. The use of barium sulfate as a liquid marker revealed a correlation between the time of the first occurrence of G-IMC and GI transit. However, the use of this marker could not demonstrate a relationship between upper GI motility and transit of this marker. The use of a solid marker as a solid meal revealed a good correlation between emptying from the stomach and transit through the small intestine and the occurrence of G-IMC. It appears that G-IMC plays an important role in transporting gastric juice and old mucous membrane and, therefore, that the early induction of G-IMC will promote early recovery from postoperative ileus.

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