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Review Article

Gastrointestinal Motility After Digestive Surgery

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Abstract
Gastrointestinal (GI) motility dysfunction is a common complication of any abdominal surgical procedure. During fasting, the upper GI tract undergoes a cyclic change in motor activity, called the interdigestive migrating motor contraction (IMC). The IMC is divided into four phases, with phase III having the most characteristic activity. After digestive surgery, GI motility dysfunction shows a lack of a fed response, less phase II activity, more frequent phase III activity of the IMC, and some phase III activity migrating orally. Postoperative symptoms have been related to motor disturbances, such as interrupted or retrograde phase III or low postprandial activity. The causes of GI disorder are autonomic nervous dysfunction and GI hormone disruptions. The administration of a motilin agonist can induce earlier phase III contractions in the stomach after pancreatoduodenectomy. For nervous dysfunction, an inhibitory sympathetic reflux is likely to be important in postoperative motility disorders. Until recently, treatment for gut dysmotility has consisted of nasogastric suction, intravenous fluids, and observation; however, more effective treatment methods are being reported. Recent discoveries have the potential to decrease postoperative gut dysmotility remarkably after surgery.

Key words Motility · Digestive surgery · Postoperative symptom · Phase III

Introduction

Postoperative disturbances of gastrointestinal (GI) function are the most common side effects of abdominal surgery. In fact, GI motility dysfunction may result after any type of abdominal surgical procedure. Postoperative ileus occurs primarily after digestive surgery in most patients and even after it resolves, patients will experience a change in GI functions. GI motor disorder is one of the causes of postprandial ileus, stasis, constipation, diarrhea, gastroesophageal reflux, Roux-Y stasis syndrome, and cholecystolithiasis. Thus, postoperative gut dysmotility is likely to persist in patients for a long time after digestive surgery.

The GI tract in healthy people has distinct contractile patterns with and without food. GI motility is divided clearly into two phases: the interdigestive state and the postprandial state. During the interdigestive state, the GI tract exhibits a characteristic motor pattern called interdigestive migration motor contraction (IMC).[1,2] The IMC consists of four phases with a combined duration of about 100 min (Fig. 1). Phase I is a quiescent period; phase II is intermittent contractions; phase III exhibits intense, rhythmic contractions that begin in the gastric body and propagate to the small intestine; and phase IV is intermittent contractions following phase III. It is thought that the physiological role of the IMC is to expel undigested food particles, mucus, and sloughed epithelial cells from the stomach or small intestine. A meal interrupts this well-defined pattern and triggers phasic contractions of variable intensity, which occur almost continuously (Fig. 2). However, the gastric fundus relaxes after eating and gastric accommodation in response to gastric distension is mediated by the stimulation of gastric mechanoreceptors.

Some surgeons accept the first passage of flatus as a clinical sign of recovery from postoperative motor dysfunction; however, earlier studies might have failed to detect the clinical changes, and assumed that bowel sounds, flatus, and GI secretion corresponded to the recovery of GI motility. Studies that evaluated GI motility found a close relationship between the motor activities of the gastrointestine and GI physical function after

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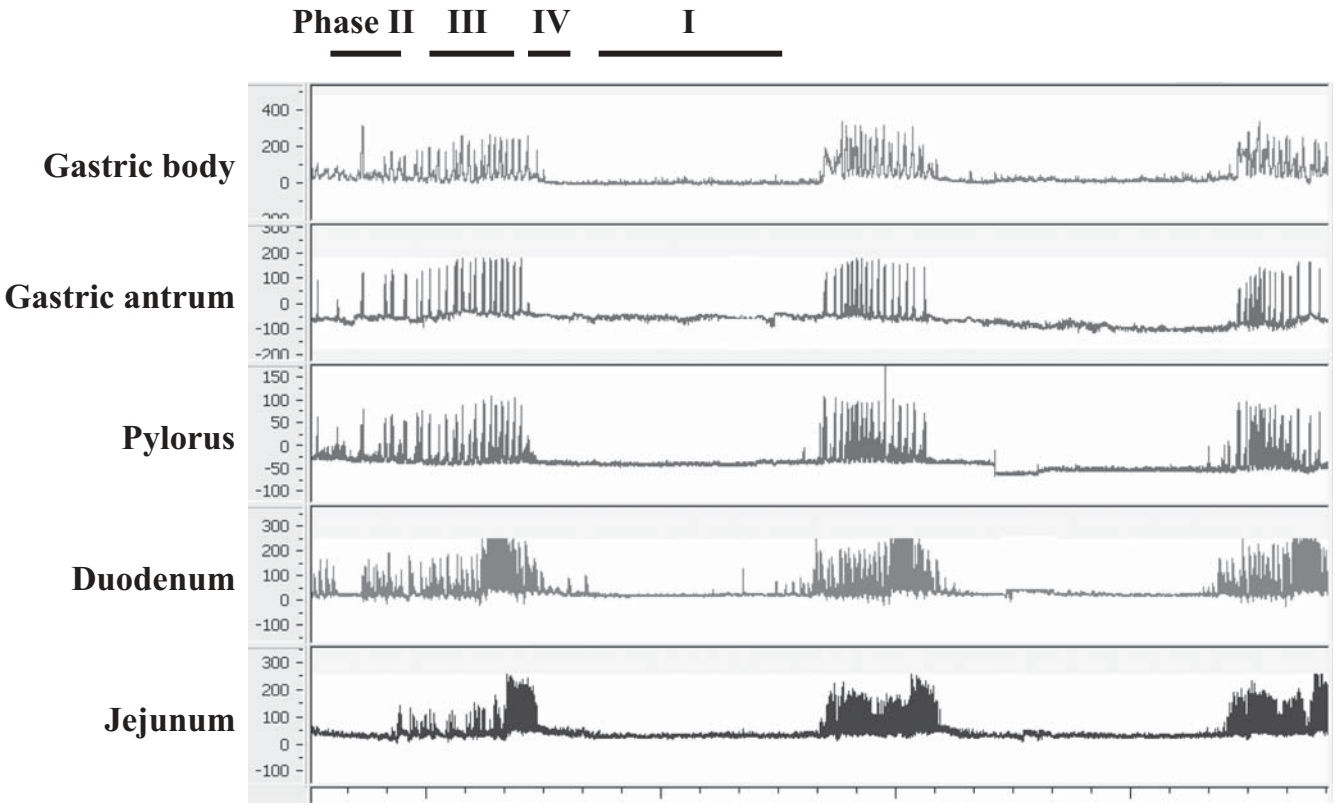

Fig. 1. Interdigestive migrating motor contractions (IMC). In the interdigestive state, IMC begin in the stomach and progress to the jejunum. This cyclic motor pattern occurs about every 90–100 min

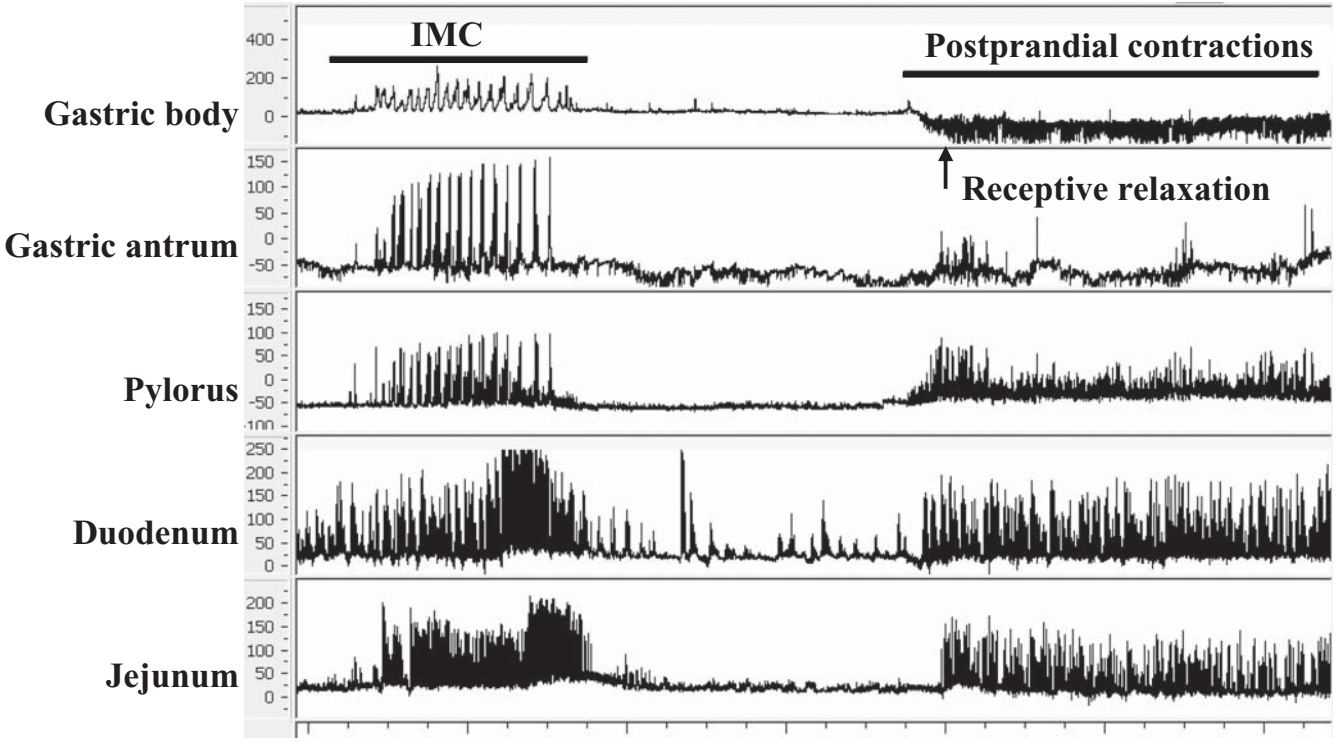

Fig. 2. Postprandial contractions. The gastrointestine generally shows irregular contractile activity within a few minutes after a meal

digestive surgery. Symptoms following gastric and small bowel surgery have been related to motor disturbances, such as interrupted or retrograde phase III or low postprandial activity.[3] After pancreatoduodenectomy (PD), motor anomalies have been detected both in the afferent and in the efferent limbs, with confirmed anomalies of phase III in the efferent limb, and decreased amplitude of postprandial activity.[4,5] In this article, we reviewed the subject of GI motor abnormalities after digestive surgery.

Esophagectomy

The stomach is the organ most frequently used to restore intestinal continuity after esophagectomy. Esophagectomy, necessitating vagotomy, results in impaired motility and delayed gastric emptying of solids, but more rapid emptying of liquids. The misconception that the gastric tube is just an inert organ and that swallowed material simply flows down with gravity has been dispelled. It is now accepted that it can contract and demonstrate motor activity. Bonavina et al.[6] examined gastric function after esophagectomy manometrically in fasting patients and concluded that the transposed stomach acts like an inert tube. Del Poli et al.[7] reported radiographic, manometric, and scintigraphic findings on 34 patients with gastric interposition, and concluded that the transposed stomach was devoid of motility and that emptying was dependent on gravity. Walsh et al.[8] reported that the vagally denervated, transposed stomach is not an inert tube but a dynamic conduit. Collard et al.[9] recently showed that the motor activity of the denervated whole stomach recovers slowly over 3 years. Furthermore, Nakabayashi et al.[10] reported that the motor activity of the gastric tube after esophagectomy slowly normalizes in a progression over time from the pylorus cephalad. Recovery of motor functions of the gastric tube is a slow process that takes years. Because the systems that organize both motor and secretory functions of the stomach are located within the myenteric and submucosal plexuses in the gastric wall, the stomach is capable of recovering its function in synchronization with the progressive disappearance of the initial ultrastructural changes in the intramural ganglionic cells.[11,12] Resection of the proximal 75% of the lesser curvature for tubulization obviously destroys some of the organizer and effect of the contractions. With time, the amplitude of contractions increases, and peristalsis and IMC reappear. The construction of a gastric tube provides a functional replacement for both the esophagus and the stomach and gives the recipient a good quality of life (QOL).

Delayed gastric emptying is estimated to occur in 40%–50% of patients,[13,14] and when it is severe, medical therapy is instituted, usually with limited success. For most patients, gastric emptying is decreased in the supine position and increased in the sitting or upright position for 3–12 months after esophagectomy.[6,15] Analysis of the motor response to food ingestion indicates that motor recovery after extrinsic denervation is far from complete: unlike the intact stomach, the gastric transplant reacts poorly to the arrival of food material into its lumen. Fed motor activity is thus more dependent on vagal impulses than motor activity in the fasting state.[12] Another possible reason for delayed gastric emptying in a linear pattern is that the reservoir function of the gastric body decreases as a result of impairment of the gastric adaptive relaxation, and the gastric volume and the mixing function of the antrum also decrease.[10]

Gastrectomy

Recent progress in the diagnosis and surgical treatment of gastric cancer has remarkably reduced mortality rate; however, more focus should be directed toward symptom relief to improve the QOL of survivors. After distal gastrectomy (DG), some patients suffer from dumping syndrome, gastritis of the remnant stomach, reflux esophagitis, stomal ulcer, and gastric stasis (Table 1). After Billroth I gastrectomy, the remnant stomach does not usually contract, and the duodenal contractile patterns influence gastric emptying (Fig. 3).[16] Gastric resection, truncal vagotomy, and interruption of gastroduodenal continuity may all be involved in inducing motor abnormalities in the GI tract. After DG, the duration of the fed pattern is shorter, and the motor response to a meal is decreased in most patients.[17] The long-term complications of gastric surgery, such as steatorrhea and diarrhea, may be the result of abnormal proliferation of bacteria in the upper intestinal tract.[18] Gastric stasis and a reduction of acid production are also possible mechanisms for bacterial overgrowth in the upper intestinal tract.[19] Bacterial overgrowth is triggered by intestinal motility disorders. It has been

Table 1. Manifestations of postgastrectomy syndrome caused by gastrointestinal dysmotility

Postoperative ileus
Duodeno-gastro-esophageal reflux
Stasis of the remnant stomach
Roux-en-Y stasis syndrome
Dumping syndrome
Stomal ulcer
Bacterial overgrowth
Cholecystolithiasis
Diarrhea
Constipation

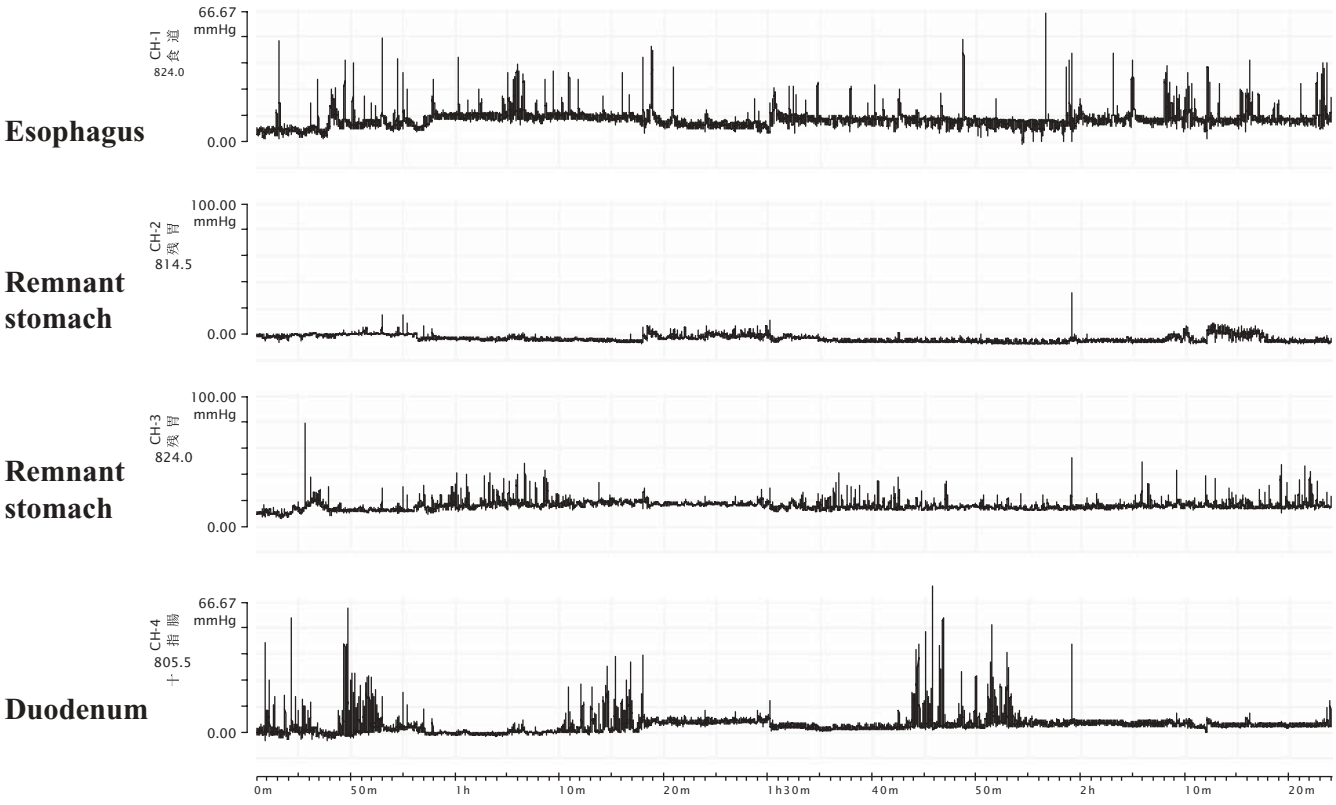

Fig. 3. Gastroduodenal motility after distal gastrectomy. Motor activity of the remnant stomach is inhibited. Interdigestive motor activity can be seen in the duodenum but not in the remnant stomach

hypothesized that IMC can no longer fulfill their "housekeeper" function.

After total gastrectomy, the digestive circuit can usually be restored by Roux-en-Y reconstruction. This procedure is effective for preventing the reflux of biliary and pancreatic juices into the esophagus, but some patients suffer a symptom complex of nausea, vomiting, and postprandial abdominal pain, known as the Roux-en-Y stasis syndrome.[20] The Roux-en-Y limb acts as an area of functional obstruction, leading to upper gut stasis and its accompanying symptoms.[21] Some studies have shown that phase III propagation is disturbed, being interrupted or retrograde in about 50% of patients. Moreover, the number of segmental contractions in the limb is increased, whereas the length of propagation is decreased.[22] Postprandial activity can also be shortened and reduced in amplitude.[21,23] These motor abnormalities seem to be caused by the interruption of intrinsic myoneural continuity, resulting from transection of the small intestine.[24,25] When symptoms are severe, prokinetics, such as bethanechol chloride and metoclopride hydrochloride, are of limited value, but shortening of the efferent limb may offer symptomatic relief.[26,27] Pacing of the efferent limb has also been tentatively applied.[28] Altomare et al.[29] reported that oral erythromycin resulted in a remarkable improvement of symptoms following Roux-en-Y gastrectomy. However, they also reported observing no differences after giving erythromycin to patients who had undergone Roux-en-Y gastrectomy. This may be because the afferent branch of the Roux limb, with a pacesetter of higher frequency than the jejunal limb anastomosed to the esophagus, interferes with motility distally, causing antiperistaltic contractions in the jejunum and esophageal reflux. This situation would be exacerbated by erythromycin.

Although total gastrectomy is widely performed for gastric carcinoma, there is no general agreement about ideal reconstruction. To provide reservoir function and to improve nutritional conditions, many types of jejunal pouch reconstruction have been described and evaluated.[30,31] Pouch function and QOL after restoration of intestinal continuity using a pouch reconstruction remain controversial. Mochiki et al.[32] reported that manometric investigations revealed major motor abnormalities in the jejunal pouch in both the fasting and fed states. In comparison with the interposed jejunum without a pouch, the motility pattern of the pouch showed reductions in overall activity and coordination among the different motility phases. Endo et al.[33] reported that patients with a higher percentage of con-

tractile bursts in the pouch had fewer postoperative symptoms, indicating that motility of the pouch could influence its postoperative function and the patient's QOL. Thus, motility in the pouch and jejunum limb may contribute to pouch function and constitute an important determinant of clinical outcome.

Pylorus-preserving gastrectomy (PPG) was first performed by Maki et al.[34] in 1967 to treat gastric ulcers. Various investigators have reported that PPG is superior to Billroth I gastrectomy because postoperative dumping syndrome is eliminated, and the procedure provides for better physiologic function of the gastric remnant.[35,36] Resection of the antrum should have an impact on gastric emptying because antropyloroduodenal coordination is an important factor in controlling transpyloric flow. Pyloric relaxation was observed only during phase III of the IMC, and it was synchronized by strong contractions of the antrum, which was accomplished by cessation of contractions of the duodenum.[37] Pyloric relaxation is thought to aid in the expulsion and interdigestive state of large particles that do not transverse the pylorus in the postprandial state. However, gastric stasis was observed during the early postoperative period after PPG, which Nakabayashi et al.[38] attributed to tonic and phasic contractions of the pylorus, as a result of transection of the wall of the stomach itself, and not because the pyloric branch of the vagus is severed. Imada et al.[36] studied solid gastric emptying with sulfamethizole capsules, given 1 month and then 1 year after surgery, and found that PPG patients had similar gastric emptying to controls, whereas conventional DG patients had significantly faster gastric emptying than the controls. Nishikawa et al.[39] also reported that liquid gastric emptying was accelerated during the early postprandial period after PPG and DG, whereas solid emptying was accelerated only after DG, and a normal solid gastric emptying pattern was seen after PPG. If gastric stasis after PPG can be improved, it may become a standard operation for patients with early gastric cancer located in the middle third of the stomach.[40]

Biliary Tract and Pancreatic Surgery

About 30%–40% of patients who undergo PD according to Whipple's procedure suffer postoperative symptoms of delayed gastric emptying or a dumping syndrome, which severely impair their QOL.[41,42] After experimental PD motor anomalies with slow phase III activity, a reduced fed pattern was seen both in the fasted and fed state.[43] A study in humans confirmed anomalies of phase III in the efferent limb with low amplitude and frequency, and interrupted propagation in 70% of the patients and decreased amplitude of postprandial activity.[5] When the head of the pancreas is resected, the surgical procedure interrupts the intrinsic circuitry and removes the duodenum where the pacemaker controlling the motor activity of the bowel is located.[44] This surgical procedure also disturbs circulating hormones. Tanaka et al.[45] reported that resection of the canine duodenum, which is known to be the principal region for motilin secretion, impaired the cyclic increase in plasma motilin concentrations and abolished the occurrence of gastric phase III activity. Furthermore, fed pattern abnormalities were explained by the significant decrease in gastrin, cholecystokinin, and insulin; all hormones involved in the onset of a fed pattern.[42,46]

Pylorus-preserving pancreatoduodenectomy (PPPD) was proposed by Traverso and Longmire[47] in 1978 to prevent the complications of standard PD, caused by reduced gastric volume, and to improve the postoperative nutritional state.[47] PPPD has now become the standard procedure for various types of periampullary diseases.[48–50] However, early gastric stasis occurs in 30%–50% of patients undergoing PPPD, causing prolonged loss of large amounts of gastric juice, delayed resumption of oral intake, and extended hospitalization.[48–51] The possible factors responsible for gastric stasis after PPPD are ischemic and neural injury to the antropyloric muscle,[52] gastric dysrhythmia,[53] and gastric atony after resection of a duodenal pacemaker, or the reduced circulating levels of motilin.[54] The duodenum plays an important role in initiating the gastric migrating motor complex and in coordinating interdigestive GI motor activity, possibly by the release of motilin.[45,55,56] Naritomi et al.[54] showed slower recovery of gastric phase III and lower plasma concentrations of motilin in patients who underwent PPPD than in those who underwent duodenum-preserving pancreatic head resection. They reported that the mean period until recovery of gastric phase III after PPPD was 30–40 days.[57–60] Conversely, another study reported that damage to the vagal branches caused transient impairment of gastric motility after PPPD.[60] Damage to the vagal nerves is reported to induce gastric dysrhythmia, particularly tachygastria, which is considered to be associated with impaired gastric IMC.[61] Thus, gastric dysrhythmia caused by damage to the vagal branches may play a role in the delayed recovery of gastric phase III after PPPD.[59,62]

The previous treatments for gastric stasis after PPPD included prolonged nasogastric tube decompression, administration of H2-receptor-antagonists, and parenteral or enteral nutritional support. Yeo et al.[41] reported on the successful use of erythromycin, a motilin agonist, to improve gastric emptying after PPPD. Furthermore, an exogenously administered motilin, leucine 13-motilin, induced phase III-like contractions and reduced gastric

juice output from a gastrostomy tube.[57] Leucine 13-motilin also induced phase III-like gastric contractions but no jejunal contractions in patients after PPPD.[57] Matsunaga et al.[57] suggested that disruption of intrinsic neural continuity across the duodenojejunostomy may explain this phenomenon.

Colorectal Surgery

The motility patterns of the colon are much more complicated than those of the upper GI tract and included segmental contractions, contractions propagating in both orad and aborad directions, and giant migrating contractions.[63–67] Sarna et al.[64] reported that the basic pattern of contraction in the canine colon consists of a quiescent state and a contractile state.[64] They defined two patterns of contractile activity: colonic migrating motor complexes (CMMC) and colonic non-migrating motor complexes (CNMC). Colonic motility is only enhanced by the ingestion of meals, and CMMC and CNMC are present even after feeding.[68–71] This reactive increase in colonic motility is called the gastrocolonic response. Shibata et al.[72] reported that the gastrocolonic reflex was mediated by capsaicin-sensitive neural pathways through a vagal reflex. Some studies reported that the 5-HT3 receptor antagonist inhibited the gastrocolonic response after a meal, indicating that a 5-HT3 mechanism participated in the physiologic contractile responses of the colon after the meal.[73,74]

Patients who undergo subtotal colectomy usually suffer from diarrhea in the early postoperative period, which gradually abates, probably because of an increase in the absorption area and an improvement in intestinal motility. Jimba et al.[75] reported that the gastric jejunal phase I changed into irregular contractions that accumulated in a regular pause, and that phase I gradually became clear after colectomy. This suggests that recovery of GI motility plays a role in the reduction of moisture volume in the intestinal matter.

Low anterior resection (LAR) and anterior resection (AR) are the operations of choice for most patients with mid- or low-rectal cancer; however, both of these operations are associated with the functional problems of increased frequency and urgency of defecation, as well as incontinence. These problems are thought to result from the loss of normal reservoir function of the proximal site of the anastomosis, a reduction in anal pressure, and colonic motility changes after surgery.[76–78] Transection with anastomosis in the pelvis is considered to influence colonic motility after LAR. Ishikawa[79] reported that denervation of the pelvic plexus caused a change in motility of the proximal colon. The neural pathway from the pelvic plexus to the proximal colon may be interrupted after these operations, even when the pelvic plexus is preserved, because the neural continuity between the pelvic plexus and proximal colon through the rectal myenteric plexus is disrupted by the rectal resection. In their studies on dogs, Tanabe et al.[80] reported that the decreased duration of colonic contractile activities of the colon and rapid propagation of CMMC, together with diminished CNMC, after the denervation + transection of colon could result in impaired specific functions in each part of the colon, such as absorption of water in the proximal colon and the storage of feces in the distal colon. Other investigators also reported that patients who underwent LAR experienced a postprandial increase in colonic activity caused by the hypersensitivity to the gastrocolonic reflex in humans.[74] These changes in colonic motility may explain the changes in postoperative bowel habits.

Prokinetic Agents and Treatment for Gut Dysmotility

The prokinetic drug cisapride is devoid of antidopaminergic effects, but acts through serotonin 4 receptors, causing the release of acetylcholine from the myenteric plexus, thereby stimulating GI motility.[81] Cisapride is effective for decreasing the duodeno-gastro-esophageal reflux (DGER) and its associated symptoms in patients with an intact stomach.[82] In fact, cisapride offered the first successful medical therapy for DGER in post-gastrectomy patients.[83] Furthermore, four of nine randomized studies found that cisapride reduced ileus significantly.[84] In normal human subjects, stimulation of intestinal motility by cisapride occurs with accelerated intestinal transit.[85] Therefore, cisapride might be useful in the treatment of functional disorders after Roux-en-Y reconstruction.[19] Unfortunately, this drug was withdrawn from the market following several incidences of cardiac arrhythmia in treated patients. Currently, mosapride, a serotonin 4 receptor agonist, is being given instead of cisapride (Table 2).

The effects of erythromycin, a macrolide antibiotic drug, and its derivatives on the motility of the GI tract, have been studied experimentally and clinically over the past 20 years. Intravenous infusion of erythromycin, which is also a motilin agonist agent, was found to induce gastric phase III, which migrates through the small intestine, in humans and dogs.[86,87] Erythromycin has a prokinetic effect on the lower esophageal sphincter, stomach, gallbladder, and small intestine.[86–90] The availability of this drug is of major importance for patients with postoperative or acquired disturbances of GI motility and transit, after conventional therapy has proved ineffective. However, the mechanism by which erythromycin acts on GI motility is not completely understood and it remains controversial. One investigator suggested that erythromycin binds directly to motilin

Table 2. Effects of prokinetic drugs and treatments for gut dysmotility

Metoclopramide	Dopaminergic blocking
Erythromycin	Motilin agonist
Cisapride	Serotonin 4 agonist
Mosapride	Serotonin 4 agonist
Daiken-chu-to	Herbal medicine
Neostigmine	Increasing parasympathetic activity
Trimebutine	Opiate modulator
Laxatives	Laxative effect
Epidural analgesia	Chemical sympathectomy
Abdominal massage	Stimulation from somatic afferent nerve
Gum chewing	Cephalic-vagal reflex
Early feeding	Intestinal reflex

receptors on GI smooth muscle,[91] whereas others reported that it acts indirectly through a cholinergic pathway.[92] Motilin receptors have recently been detected in enteric neurons in humans.[93] Attempts to exploit the prokinetic effects of erythromycin have met with varying success.[10,12,40,58] Some investigators reported that erythromycin decreased certain upper GI symptoms in gastrectomized patients by enhancing GI transit or gastric emptying.[29,94,95] One prospective, randomized, placebo-controlled, double-blinded study showed that erythromycin accelerated gastric emptying significantly after pancreaticoduodenectomy and reduced the incidence of delayed gastric emptying.[41] The obvious limitation of its involvement is that, as an antibiotic, it may result in disturbance of the intestinal flora with subsequent GI upset.

Dai-kenchu-to extract powder is a mixture of dried ginger root, ginseng, and zanthoxylum fruit in the ratio of 5:3:2, respectively. Intragastric Dai-kenchu-to induced phasic contractions in the antrum, duodenum, and jejunum of dogs.[96] This extract has been used conventionally for abdominal distension in Japan and recently was reported to be effective against intestinal obstruction after laparotomy and against irritable bowel syndrome.[97] Endo et al.[98] reported that Dai-kenchu-to increased pouch contractions after total gastrectomy with jejunal pouch interposition and decreased postoperative stasis-related symptoms.[98]

Postoperative ileus is common after abdominal operations and can result in the accumulation of secretions and gas, with nausea, vomiting, abdominal distension, and pain. The causative mechanisms of postoperative ileus are considered to be multifactorial, but it is generally believed that the major contributors are activation of the inhibitory neural reflex pathways and inflammatory processes. Asao et al.[99] reported faster return of bowel function and a trend toward earlier hospital discharge in patients who chewed gum after laparoscopic colectomy. Gum chewing is postulated to activate the cephalic-vagal reflex, which is usually enhanced by food, and to increase the production of GI hormones associated with bowel motility.

Search Strategy

Recent data for this review were collected by Medline searches.

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