

The effect of continuous jejunal interposition on gastrointestinal hormones after distal gastrectomy

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ABSTRACT

The objective of our study was to determine the effect of continuous jejunal interposition on gastrointestinal hormones after distal gastrectomy, and lay a foundation for surgical management.

Distal subtotal gastrectomy experimental model were established on 24 adult Beagle dogs. Digestive tract reconstruction of the dogs was randomly divided into continuous jejunal interposition group, Billroth II anastomosis group and isolated jejunum interposition group. The content of serum gastrin, plasma motilin and cholecystokinin after different digestive tract reconstructions was detected and compared by enzyme-linked immunosorbent assay.

In the dogs which received continuous jejunal interposition, postoperative serum gastrin level was significantly lower than before surgery either in fasting or postprandial state (all $p < 0.05$). The serum gastrin level of continuous jejunal interposition group was significantly higher than the other groups in postprandial state (all $p < 0.05$), and was significantly higher than Billroth II -type anastomosis group in fasting state ($p < 0.05$). Furthermore, the postoperative plasma motilin and cholecystokinin levels were significantly higher than before surgery either in fasting or postprandial in dogs received continuous jejunal interposition (all $p < 0.05$). The postoperative plasma motilin level of continuous jejunal interposition group was significantly higher than the other groups in postprandial state (all $p < 0.05$), and was significantly higher than Billroth II -type anastomosis group in fasting state ($p < 0.05$). However, the postoperative cholecystokinin level of continuous jejunal interposition group was significantly lower than the other groups (all $p < 0.05$).

Continuous jejunal interposition after distal gastrectomy could maintain the postoperative plasma motilin and serum gastrin in a relatively high level, while cholecystokinin in a low level.

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KEY WORDS: distal gastrectomy, continuous jejunal interpositionon, serum gastrin plasma motilin, sholecystokinin

INTRODUCTION

The survival of patients with gastric cancer has recently been improved because of early detection, rational lymphadenectomy and several therapeutic modalities [1, 2]. However, gastric cancer still remains the second leading cause of cancer mortality in the world. At present, it is acknowledged that operation and systemic chemotherapy can clearly improve the survival of patients with gastric cancer [3, 4]. Besides survival, patients are increasingly expecting high quality of life post operation at present [5, 6]. However, the studies based on postoperative gastrointestinal function recovery based on experimental models are still sparse. It was acknowledged that gastrointestinal hormones play important role in the regulation of gastrointestinal function [7, 8]. However, the

effect of different interpositionon methods on gastrointestinal hormones after distal gastrectomy is still unclear [9, 10]. The Billroth I procedure for gastroduodenostomy is the most physiologic type of gastric resection, since it restores normal continuity [11, 12]. However, in clinical practice, Billroth I procedure is not likely to be suitable for the cases with large tumors due to the anastomotic tension. Furthermore, postoperative reflux also greatly impacts the quality of life after treatment. On the other hand, Billroth II and isolated jejunum interposition reconstruction methods are welcomed in the cases occur anastomotic tension while these procedures bring many post-operative complications such as bile reflux, anastomotic ulcer, gastric stump cancer and so on [13]. Roux-en-Y reconstruction seems to be the most often performed clinically, as this procedure is simple, safe and has acceptable postoperative complications [14, 15]. However, there are still some common problems such as dietary restriction, early satiety, postprandial fullness, vomiting, heartburn, dumping syndrome and diarrhea, because of loss of reservoir function as well as disturbance of digestion after gastrectomy. We designed a new type of gastrointestinal tract reconstruction

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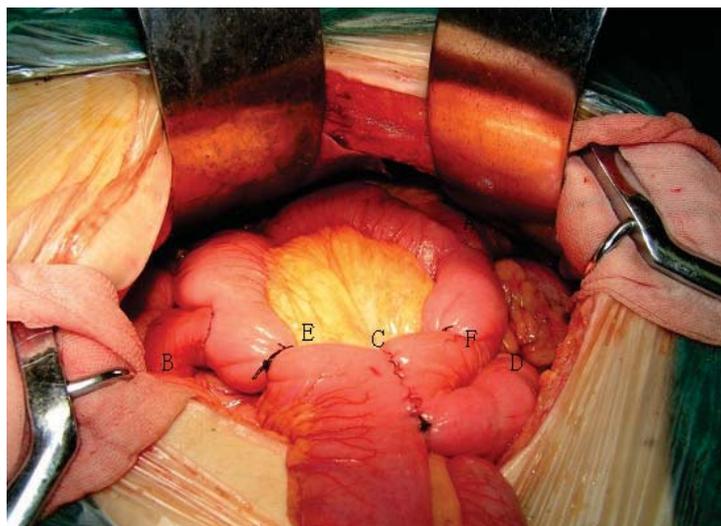
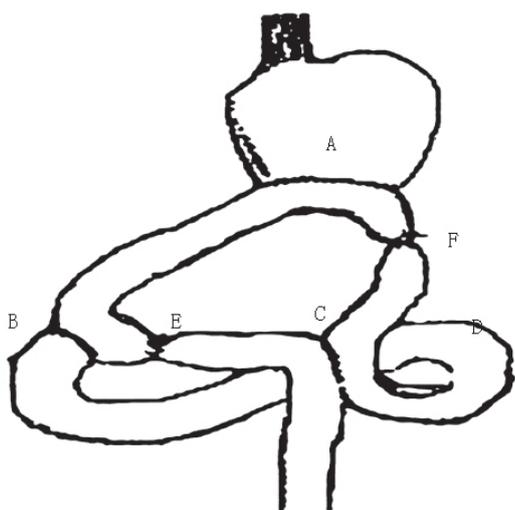


FIGURE 1. Integral continual jejunal interposition. A. gastrojejunostomy, B. duodenojejunosomy, C. side-to-side jejunostomy, D. Treitz's ligament, and E. and F. the ligation sites.

method and have achieved good outcomes since 2002 (Figure 1). In order to gain experimental foundation, we established distal subtotal gastrectomy experimental model and investigated the effect of continuous jejunal interposition on gastrointestinal hormones compared to the other two methods.

MATERIALS AND METHODS

Experimental dogs

The study was approved by the Ethics Committee Wenzhou Medical College. Twenty-four adult Beagle dogs (7.5-9.5 kg) were randomly divided into three groups using random number table method. The three groups were performed continuous jejunal interposition, Billroth II-type anastomosis and isolated jejunum interposition digestive tract reconstruction after distal gastrectomy separately. After 24 hours fasting, the dog was induced to anesthesia by 5% pentobarbital (0.3 ml/kg) intravenous injection and ketamine (10 mg/kg) intramuscular. Then, intubation and mechanical ventilation, 1-2% isoflurane (100% oxygen inhalation) maintained anesthesia.

Operation procedure

Distal gastric was resected following the connection between the right of the first descending branch of left gastric artery and the left of the first vertical branch of big gastroepiploic left artery. Digestive tract reconstruction of the dogs was randomly divided into continuous jejunal interposition group, Billroth II-type anastomosis group and isolated jejunum interposition group. Operation procedures were as following: 1) continuous jejunal interposition group (n=9); First, gastric - jejunum end to side anastomosis were performed at 20 cm distal from the Treitz's ligament. Then, at 30 cm distal from gastric - je-

junum anastomosis, duodenum - jejunum end to side anastomosis were operated. Following, jejunum side-side anastomosis was performed at 10cm away from the distal end of the duodenum-jejunum anastomosis and 15cm away from the Treitz's ligament. At the last, closed distal jejunum 5cm away from the duodenum-jejunum anastomotic after closing the proximal jejunum at 2cm away from the stomach-jejunum anastomosis. 2) Billroth II -type anastomosis(n=7); First, closed the duodenal stump. Then, stomach - jejunum end to side anastomosis was performed in front of colon at 25-30 cm from the Treitz's ligament. 3) Isolated jejunum interposition (n=8); Select a length of 25cm interposition with mesangial as an intestinal segment at 30 cm from the Treitz's ligament (note intestinal blood supply). In front of the colon, end to end anastomosis was implemented between gastric and jejunum segment interposition. Then, anastomosis the duodenal and jejunum segment interposition. At the last, jejunum-jejunum anastomosis were performed.

Postoperative treatment

The dogs were fasting and received intravenous infusion of 5% glucose and sodium chloride containing antibiotics and vitamins (40 ml/kg/d) during the first 72 hours after operation. After operation 72 hours, the dogs started to be provided liquid diet. The period for the diet transition was depending on the situation. It will be approximately 2 weeks after operation to resume a normal diet (commercial dog food 240 g/day per dog). Unfortunately, two dogs died of peritonitis one week after operation in isolated jejunum interposition group.

Experimental sample preparation

2 ml venous blood was separately drawn from the experimental dogs which were in the fasting state as well

as 1 hour after postprandial state one month and two months after the treatment. After 4°C centrifugation, plasma were taken and put in -70 °C refrigerator. The levels of serum gastrin, and motilin and cholecystokinin were detected by enzyme-linked immunosorbent assay. The specific methods refer to the kit requirements.

Statistical analysis

All data was analyzed with SPSS statistics software (Version 13.0, Chicago, IL, USA). Independent t-tests and ANOVA were used to compare the differences between categorical and numeric variables. A *p* value of less than 0.05 was considered statistically significant.

RESULTS

In dogs received continuous jejunal interposition, postoperative serum gastrin level was significantly lower than before surgery either in fasting or postprandial (*p*<0.05). The serum gastrin level of continuous jejunal interposition group was significantly higher than the other groups in postprandial (all *p*<0.05), and was significantly higher than Billroth II -type anastomosis group in fasting (*p*<0.05) (Table 1). Furthermore, the postoperative plasma motilin and cholecystokinin levels were significantly higher than

TABLE 1. Changes of serum gastrin levels after treatment in different groups (ng/L, x±S).

		Pre-operation	One month after treatment	Two months after treatment
Billroth II anastomosis group	fasting state	3.86±0.96	1.78±0.57	1.72±0.61
	postprandial state	4.86±0.96	2.48±0.87	2.68±0.97
Isolated jejunum interposition group	fasting state	3.78±1.13	1.99±0.54	1.95±0.73
	postprandial state	4.988±1.73	2.98±0.81	3.78±0.63
Continuous jejunal interposition	fasting state	3.75±1.02	2.18±0.63	2.16±0.67
	postprandial state	5.33±1.79	3.05±0.73	3.88±0.75

TABLE 2. Changes of plasma motilin levels after treatment in different groups (ng/L, x±S).

		Pre-operation	One month after treatment	Two months after treatment
Billroth II anastomosis group	fasting state	430.6±128.3	503.9±168.6	496.8±157.3
	postprandial state	849.0±208.6	981.6±258.4	839.5±204.6
Isolated jejunum interposition group	fasting state	442.0±131.6	557.2±171.5	549.3±198.6
	postprandial state	852.3±213.8	1005.0±293.5	996.0±198.6
Continuous jejunal interposition group	fasting state	428.6±127.5	583.0±198.2	577.1±203.6
	postprandial state	853.7±218.3	1068.7±305.9	1002.5±208.6

TABLE 3. Changes of plasma cholecystokinin levels after treatment in different groups (ng/L, x±S).

	Pre-operation	One month after treatment	Two months after treatment
Billroth II anastomosis group	18.86±2.07	22.37±2.98	22.16±2.13
Isolated jejunum interposition group	18.91±1.93	20.24±2.53	20.05±2.49
Continuous jejunal interposition group	18.98±2.03	19.82±2.11	19.63±2.01

before surgery either in fasting or postprandial in dogs received continuous jejunal interposition (all *p* <0.05). The postoperative plasma motilin level of continuous jejunal interposition group was significantly higher than the other groups in postprandial (all *p*<0.05), and was significantly higher than Billroth II -type anastomosis group in fasting (*p*<0.05) (Table 2.). However, the postoperative cholecystokinin level of continuous jejunal interposition group was significantly lower than the other groups (all *p*<0.05) (Table 3.).

DISCUSSION

Gastric cancer remains a major cause of cancer death, and the 5-year survival rate in patients with gastric cancer is still poor despite improved survival due to early detection, rational lymphadenectomy and several therapeutic modalities [16, 17]. Nowadays, the expectation of high quality of life (QOL) after operation is increasing. However, postoperative complications after gastrectomy still seriously impact the quality of life (QOL) of patients though surgical methods have been improved in the past decades [18]. There is increasing evidence that the changes of gastrointestinal hormones play an important role in the gastrointestinal function after operation. However, the studies investigating the effect of different gastrointestinal reconstruction methods on gastrointestinal hormones after distal gastrectomy on experimental model are still sparse [10]. We designed a new type of gastrointestinal tract anastomosis and have achieved good results since 2002 [19, 20]. In order to gain experimental foundation, we performed continuous jejunal interposition in experimental dogs and investigated whether or not an improved gastrointestinal hormone level and good clinical course was observed. The propulsion of gastrointestinal contents depends on the peristalsis of the gastrointestinal smooth muscle. Spontaneous depolarization in this muscle (slow wave or the basic electrical rhythm) leads to the production of action potential spikes. These excite spontaneous peristalsis, which is modified by the action of chemical factors, nerves and gastrointestinal hormones. Gastrointestinal hormones are secreted by the scattered endocrine cells on the wall of the gastrointestinal tract and pancreatic islet cells to

secrete. The main function of gastrointestinal hormones is to regulate movement, secretion and absorption of digestive organs collaborated with the nervous system [21]. In our study, the postoperative serum gastrin level of dogs received continuous jejunal interposition was significantly lower than before surgery either in fasting or postprandial state. The gastrin secretion reduced maybe due to the resection of antrum. To be interest, the postoperative plasma motilin levels were significantly higher than before surgery. It may be a compensatory reaction of the body after operation. The serum gastrin level of continuous jejunal interposition group was significantly higher than the other groups in postprandial, and was significantly higher than Billroth II -type anastomosis group in fasting state. After resecting gastric antrum, gastrin was mainly from the duodenum. However, the duodenal mucosa undergoes atrophy lacking of excitement in the gastrointestinal anastomosis in which the food dose not pass through the duodenum. The duodenum was excused in Billroth II -type anastomosis groups, hence, the number of G cells and M cells reduced due to the duodenal mucosa atrophy. As a result, the secretion of gastrin and plasma motilin was significantly reduced. However, continuous jejunal interpositionon successfully resolved the problem. The continuous jejunal interpositionon retained the duodenum function in greatest degree and was effectively against the atrophy of duodenal mucosa. Furthermore, Johnson et al. [22] founded that transection and reanastomosis of the intestinal wall changes the temporal and spatial organization of contractions distal to the transection site. The continuous jejunal interpositionon retained not only the continuity of the digestive tract but also the nerve - muscle continuity, hence, the intestinal nerve system maintained its' integrity. After investigating the differences in gastrointestinal hormone production at 3 different reconstruction types after total gastrectomy, Kalmár et al. [23] founded that pancreatic secretion was not synchronized with the meal. Irregular food entering speed and sequence and gastrointestinal andsecretory dysfunction could easily result in pancreatic exocrine insufficiency which promoted the secretion of cholecystokinin. But the gastrointestinal reconstructions which preserved duodenum pathway successfully avoided this problem. In this study, the postoperative cholecystokinin level of continuous jejunal interposition group was significantly lower than the other groups. As maintained successive intestinal patency, continuous jejunal interposition group got low impact on intestinal and pancreatic secretory function compared to isolated jejunum interposition group. Hence, cholecystokinin kept in a relatively low level.

CONCLUSION

In conclusion, continuous jejunal interpositionon on gastrointestinal hormones after distal gastrectomy kept relative high levels of serum gastrin and plasma motilin, meanwhile mentained a low level of cholecystokinin in experimental model. In clinical practice, continuous jejunal interpositionon was observed fewer surgical complications and mortality compared with Billroth II anastomosis group and isolated jejunum interposition group. However, recommendation of a new surgical approach should be cautious. We expect more studies based on the topic performed to verify the security of the surgery.

DECLARATION OF INTEREST

The authors have no conflict of interest to declare.

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