Original Article
A modified protective device prevents abdominal adhesion in ghost ileostomy: a dog model

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Abstract: Objective: This study aimed to evaluate the protective effect of a new type of device for ghost ileostomy on intestinal adhesions. Methods: Thirty adult dogs were randomized into three groups including a sham-operated control group (C), traditional ghost ileostomy (T) group and ghost ileostomy with protective device group (G). In T group, ileum was subcutaneously supported by a latex ring while the ileum was fixed with protective device in G group. The ileum was put back to the abdominal cavity 14 days later, the average operative time of doing and reverse ileostomy was recorded. Adhesions were scored by Blauer and Collins score method. On postoperative day 28, dogs were sacrificed to harvest the ileum loop and regional abdominal wall. The hydroxyproline (Hyp) and tissue plasminogen activator (tPA) levels were measured by ELISA assay. Results: The ileum in group G can be reversed easily with lower adhesion score than group T (P = 0.012), as well as lower intra-abdominal macroscopic scores of adhesions (P = 0.012 < 0.05). The total fibroblastic activity and vascular proliferation in G group was lower than T group significantly (P = 0.026, 0.022 respectively). Total microscopic score and the Hyp in G group was lower than that in T group (P = 0.013). However, the tPA level in G group was significantly higher than that in T group (P = 0.021). Conclusions: The ghost ileostomy protective device safely and effectively prevented adhesions between the ileostomy loop and abdominal wall.

Keywords: Ghost ileostomy, protective device, adhesions

Introduction

Colorectal cancer remains the third most common cancer in the world [1]. Anastomotic leakage is one of the most dreaded complications after colorectal surgery which is associated with higher mortality rate (6-16% for 30-day mortality) [2]. Despite surgical advances, anastomotic leakage still ranges from 3% to 20% [3, 4].

Though protective ileostomies reduce the mortalities of pelvic sepsis after colorectal surgery, reduce the anastomotic leakage-associated complications and subsequent rate of leak-related re-intervention [5-7], protective ileostomies still increase the rate of complications such as bowel obstruction, parastomal skin irritation, parastomal herniation, prolapse, peristomal infection, abscess and fistula [8-10].

A modified form of ileostomy, known as pre-stage ileostomy (Ghost Ileostomy-GI) has been suggested recently [11, 12]. In this modified ileostomy, an intestinal loop of terminal ileum is identified, fixed to the skin with a vascular vessel loop or a pediatric Robinson catheter, ensuring adequate vascular supply. In the event of anastomotic leakage, the GI can be opened and transformed into a classical ileostomy. The loop can be repositioned into the abdominal cavity under local anesthesia conveniently if no leakage occurs. However, this modified ileostomy has not been widely used due to the adhesions between ileum loop and abdominal wall interfering with subsequent ileostomy or ileum loop reversal.

Therefore, we invented a new device (Patent No. 201420335556.1) to prevent the adhesion surgically via ileostomy or loop reversal. Furthermore, we evaluated the anti-adhesive
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Materials and methods

Experimental design

This study was carried out in the Animal Research Laboratory of Xuzhou Medical College with approval by the Animal Ethics Committee of Xuzhou Medical College. The study was carried out according to the Declaration of Helsinki and the Principles of Laboratory Animal Care.

The protective device includes a main part (4 cm × 2 cm) and two auxiliary parts (2 cm × 0.5 cm) which is able to cover preplaced ileum and attach the device to abdominal wall, respectively (Figure 1A, 1B). The device was made of silicone and could be sterilized under conventional high temperature.

A total of 30 adult dogs (body weight, 10.0-12.0 kg) were provided by the Animal Experimental Center of Xuzhou Medical College (Xuzhou, China) (license no. SCXK (Su) 2010-0003). The dogs were assigned to three groups, each containing 10 dogs. They were housed in individual cages on a 12:12 light/dark schedule under controlled temperature (21-23°C) and a relative humidity of 60-65%, with free access to standard dog diet and water. They were fasted for 12 hrs and weighed after pentobarbital (1000 mg/kg) anesthesia. Surgical procedures were performed under sterile conditions. The abdominal region was cleaned using 7.5% povidone iodine soap and saline, the area was then shaved and stained with 1% povidone iodine. A 4 cm right lower vertical abdominal incision was performed. The following treatments were implemented in each group:

Group C (control) (n = 10): A 4 cm right lower vertical abdominal incision was performed to open and close the right low abdominal wall freely touching the intestine.

Group T (traditional ghost ileostomy) (n = 10): A 4 cm right lower vertical abdominal incision was performed with the ileum subcutaneously supported by a latex ring and closing the abdominal skin layer only.

Group G (ghost ileostomy with protective device) (n = 10): A 4 cm right lower vertical abdominal incision was performed. The ileum was fixed using the protective device subcutaneously and closing the abdominal skin layer.

Fourteen days after surgical intervention, the dogs were anaesthetized and the ileum was put back. The average operative time of doing and reverse ileostomy was recorded. The intra-abdominal adhesions and other abnormalities were also examined carefully. Adhesions were scored by pathologist, who was blinded to the groups, according to the Blauer and Collins...
score method [13] as following: 0: no adhesion; 1: thin adhesive bands, easily removable; 2: thick adhesive bands limited to one area; 3: extensive and thick adhesive bands; and 4: extensive and thick adhesive bands, adhesions between viscera and/or abdominal wall. On postoperative day 28, dogs were sacrificed, weighed, their abdomen was opened in a U-shaped incision, the ileum loop and regional abdominal wall were harvested together. The samples were placed in an airtight tube and kept frozen at -80°C until the histopathological examination and laboratory analysis. All measurements were conducted when animals were alive and anaesthetized.

Histopathology

Samples were fixed in 10% formalin and embedded in paraffin, and 5-μm cross-sections were prepared using a microtome, followed by haematoxylin and eosin (H&E)-staining and visualization under light microscope. The samples were scored for fibrosis, inflammation and vascular proliferation. Fibrosis was scored as follows [14]: 0: no fibrosis; 1: minimal, loose fibrosis; 2: medium degree fibrosis; 3: dense fibrosis. Inflammation was scored as follows: 0: no inflammation; 1: existence of giant cells, occasional lymphocytes and plasmocytes; 2: giant cells, plasma cells, eosinophil and neutrophils; 3: various inflammatory infiltrates and microabscesses. Vascular proliferation was scored as follows: 0: no vascular proliferation; 1: light vascular proliferation; 2: medium vascular proliferation; 3: severe vascular proliferation.

Laboratory analysis

The level of hydroxyproline (Hyp) was measured using a Hyp detection kit (μg/g) (EnoGene, China), according to the manufacturer’s instructions. The tissue plasminogen activator (tPA) (ng/g) was assayed by specific enzyme-linked immunosorbant assays (ELISA) (EnoGene, China) in accordance with the manufacturer’s instructions. The absorbance in the wells was measured at 450 nm in a microplate reader.

Statistical analysis

The data were expressed as mean ± standard deviation (SD). All experimental data was summarized from at least three independent exper-
We evaluated differences between two groups by unpaired t test and among multiple groups by one-way analysis of variance. A statistically significant difference was considered as two-tailed P value less than 0.05. Analyses were performed with SPSS 17.0 software (Chicago, IL, United States).

Results

The average operative time of doing ileostomy was (1185.00 ± 170.00 s), (1655.80 ± 143.22 s) in Group T and G, no obvious difference between the two groups (P = 0.23 > 0.05). But the reverse time in Group G (303.25 ± 87.45 s) was significantly lower than that in Group T (644.50 ± 81.82 s) (P = 0.001 < 0.05). The intra-abdominal macroscopic scores of adhesions in Group G (1.40 ± 0.84) were lower than that in Group T (2.50 ± 1.08) (P = 0.012 < 0.05). There was almost no adhesion in Group C (control group) (0 ± 0.00) (Figure 3A, 3B). During the 28 day period, one dog died of ileus in Group T (traditional ghost ileostomy group) on day 12 and one occurred an incision rupture in Group G (ghost ileostomy with our protective device group) on day 11 (Figure 2A, 2B), which were replaced with new dogs separately from the initial experiment. The weight of dogs in both groups had no significant change before and after surgery.

As shown in Figure 4, the total microscopic score of fibroblastic activity and vascular proliferation in group G (1.36 ± 0.47 and 1.28 ± 0.41, respectively) was significantly lower than that in group T (2.37 ± 0.76 and 1.91 ± 0.54, respectively) (P = 0.026, 0.022 < 0.05) (Figure 4A, 4D). The total microscopic score of inflammation in group G (1.51 ± 0.63) was mildly lower than that in group T (1.85 ± 0.86) (P = 0.418 > 0.05) (Figure 4E, 4F). The concentration of Hyp in group G (2.00 ± 0.60 µg/g) was lower than that in group T (3.64 ± 1.49 µg/g) (P = 0.013 < 0.05). The tPA level in group G (2.50 ± 0.86 ng/g) was significantly higher than that in group T (1.88 ± 0.22 ng/g) (P = 0.021 < 0.05) (Figure 5A, 5B).

Discussion

In the present study, less adhesion from gross appearance was found in group G, and the total
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microscopic score of adhesion was lower in Group G compared with that in Group T. Even the build time of the ghost ileostomy in Group G was slightly longer than that in Group T, but the reverse of the ghost ileostomy in Group G may be more easily because of less adhesion formed. In addition, the total microscopic score of fibroblastic activity, and vascular proliferation in group G was significantly lower than that in group T. This finding suggested that our protective device could decrease the degree of adhesion during ghost ileostomy.

Furthermore, our data showed that the tPA activity was higher in group G than that in group T. The Hyp level in group G was significantly lower than that in group T which suggested that our protective device significantly reduced post-operative abdominal adhesion formation. However, the total microscopic score in group G was mildly lower than that in group T, which was probably due to the absence of inadequate sample size.

Protective ileostomy is increasingly used for lower rectal cancer [2], which effectively reduces anastomotic leakage after low anterior resection below the peritoneal fold [15, 16], resulting in a reduced risk of re-intervention for anastomotic leakage or abscess. In addition to co-morbidities and the risk of mortality with the construction and reversal of protective ileostomy, a stoma presents challenges for activities of daily living, feeding and clothing, sexual activity, and is associated with the risk of failure [17-19].

There are many variables have been confirmed to be associated with the risk of anastomotic leakage. With these variables, it is easy to identify those high-risk patients who would benefit from stoma protection and those who do not require stomas with low-risk, but whether to construct a protective stoma in patients with a medium risk may be not simple [20, 21]. The overall rate of anastomotic leakage ranges from 3% to 20% [3, 4], and the rate in our unit was 10% among 884 cases in the past five years. Therefore, in about 90% of cases, the stoma may be a clinical dilemma. Unfortunately, there is no unified guideline for the surgical reconstruction until now. Most often, surgeons make decision based on personal experience.

A series of technical alternatives were described to protect ileostomy. Percutaneous ileostomy or tube ileostomy [8, 11, 22, 23], involves insertion of jejunostomy tube into the ileum about 30-40 cm proximal to the ileocaecal valve for drainage of feces. Once the integrity of anastomosis is confirmed, the probe is removed and the probe orifice heals by itself. In case of symptomatic anastomotic leakage, percutaneous ileostomy acts as a traditional loop ileostomy. However, it is not widely used due to the absence of total occlusion of ileum by the inflated balloon [24].

Ghost ileostomy, another modified approach [11, 23, 25], in which a prophylactic preplaced ileum loop attached to the right low abdominal wall was performed after low anterior rectal resection. The ileum loop may be removed on post-operative days 9-10 in case of anastomotic leakage. Otherwise, the sutures closing the incision in the right iliac fossa are removed, the intestinal loop with the pediatric Robinson catheter is exteriorized and the ileostomy is fashioned under local anesthesia. However, clinically, even with a protective film, dense adhesions between ileum loop and abdominal wall may prevent completion under local anesthesia. Collateral damage including intestinal injury, bleeding and infection, may occur during the surgery.

The pathophysiology of dense adhesions following injury to the normal peritoneal tissue is
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poorly defined. A uniformly effective method of adhesion prevention is unavailable [26]. The process of adhesion, mainly occurs within 5 to 10 days, might be regarded as an ischemic disease, which may result in peritoneal damage followed by tissue inflammation, fibrin deposition within the inflammatory exudate [27]. Disturbed equilibrium between fibrin deposition and fibrinolytic activity leads to persistent fibrinous bands followed by fibrinogen accumulation and adhesions [28]. A decrease in the release of tPA in the peritoneal mesenchymal cells plays a key role in adhesion formation [29, 30]. The Hyp level, a fibrinogen precursor, may reflect the severity of tissue adhesion.

A suitable biomaterial should be developed followed by a prospective, randomized controlled trial (RCT) to study its safety and efficacy before clinical application. Materials appropriate for the protective device shall be available. Our preliminary study has shown that this novel ghost ileostomy protective device could prevent adhesions between ileum loop and abdominal wall during colorectal surgery. In our future study, we need to expand the sample size and evaluate its effect after the second surgical intervention.

Our novel ghost ileostomy protective device appears to safely and effectively prevent adhesions between ileum loop and abdominal wall during colorectal surgery. It obviates the need for unnecessary ileostomy, leading to tremendous economic and social advantages, if widely applied in clinic.

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Disclosure of conflict of interest

None.

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