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Curative effect of laparoscopic surgery on acute gastric perforation

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ABSTRACT

Objective: To investigate the postoperative inflammatory reaction, stress reaction and immune response of laparoscopic surgery and laparotomy for acute gastric perforation.
Methods: Forty-four patients with acute gastric perforation receiving emergency surgery in our hospital from May 2012 to December 2015 were selected and retrospectively analyzed. Among these patients, there were 19 patients treated with laparoscopic surgery (LS group) and 25 patients treated with laparotomy (laparotomy group). At the first day after surgery, their serums were collected and the indexes of inflammatory reaction and stress reaction were detected. Mononuclear cells and red blood cells in peripheral blood were collected and detected for the immune function indexes.
Results: At day 1 after surgery, the contents of serum interleukin-1β (IL-1β), IL-2, IL-6, IL-8, IL-10, cortisol, norepinephrine, epinephrine, renin and angiotensin-II of patients in the LS group were all significantly lower than those of the laparotomy group; fluorescence intensities of CD3, CD4, CD16 and CD56 of mononuclear cells in peripheral blood were all obviously higher than those of the laparotomy group; and the numbers of red blood cell C3bR and immune complex resette and the fluorescence intensities of complement receptor type 3, CD58 and CD59 were obviously higher than those of the laparotomy group.
Conclusions: Emergency laparoscopic surgery used to treat acute gastric perforation shows slight postoperative inflammatory reaction and stress reaction and presents weak nonspecific immune response, specific immune response and erythrocyte immune response, which makes less trauma than laparotomy.

1. Introduction

Acute gastric perforation is a common acute abdominal disease in general surgery department. Psychentonia, overstrain and irregular diet are all responsible for gastric perforation. When the stomach or duodenum perforates, digestive juice gets into the enterocoelia via the perforation site leading to diffuse peritonitis. The development of the disease is characterized by acute onset, great damage and poor prognosis[1,2], and if it is not repaired in time, it will further result in septicopyemia and systemic inflammatory response syndrome. The severe one will develop multiple organ dysfunction syndrome and even die[3]. Emergency surgery is the preferred way used to treat gastric perforation in clinic. Subtotal gastrectomy was mostly taken in the past. However, it caused greater surgery trauma and poor living quality. In recent years, gastric perforation repair surgery has gradually replaced the subtotal gastrectomy and become the preferred way of emergency surgery to treat gastric perforation.

The laparotomy of gastric perforation repair is a traditional way of gastric perforation repair surgery. The operation field is clearly exposed and the operation is quite easy, which can effectively repair the perforation site and is widely used in the treatment of gastric perforation as an emergency surgery[4,5]. However, laparotomy leads to a greater trauma, which will cause a strong inflammatory reaction, stress reaction, and further a poor postoperative recovery of body function and inhibit the immune function as well. Laparoscopic surgery is a minimally invasive surgical way developed in recent years, which causes very little trauma when repairing gastric perforation, and provides faster postoperative recovery[6,7]. At

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present, laparoscopic repair for treating gastric perforation is widely used by more and more international and domestic academics, which achieves positive curative effects. However, situations about postoperative inflammatory reaction, stress reaction and immune response after gastric perforation repair surgery with laparoscope have not yet been reported. In the following study, we analyzed the situations of postoperative inflammatory reaction, stress reaction and immune response after treatment with laparoscopic surgery and laparotomy for acute gastric perforation.

2. Materials and methods

2.1. Study objects

A total of 44 patients with acute gastric perforation receiving emergency surgery in our hospital from May 2012 to December 2015 were selected and retrospectively analyzed. The inclusion criteria were listed as follows: (1) Patients hospitalized for great epigastric pain and their physical examinations showing tension, pressing pain and rebound tenderness on epigastrium or the whole abdominal muscle; (2) Patients diagnosed with digestive tract perforation by abdomen X-ray after hospitalization with subphrenic free air; (3) Patients diagnosed with benign lesion by postoperative pathology; (4) Informed consents were obtained from patients and their families. Among these 44 patients, 19 patients treated with laparoscopic surgery were included in the LS group, and 25 patients treated with laparotomy were assigned in the laparotomy group.

2.2. Surgery methods

Patients from both groups were conducted surgery under general anesthesia. The surgery methods for patients in the LS group were described as follows. An arc incision was made at the superior border of the umbilical cord as the main insert hole. Pneumoperitoneum was established and the pneumoperitoneum pressure was maintained at 12–14 mmHg. Trocars (1.0 cm and 0.5 cm) were placed at 3 cm below the costal margin of the left and right midline of the collarbone as operation hole. Ascites in the enterocoelia was pumped dry and then the liver was retracted. Absorbable suture was used for discontinuous full-thickness suture when the perforation site was found. After there surelly existed no leakage at the repaired part, the enterocoelia was swashed with normal saline till the washing fluid was completely absorbed, and then drainage tube could be placed in. The surgery methods of the laparotomy group were as follows. A median incision was made at the epigastrium, and conventional gastric perforation repair surgery was carried out. Then, the enterocoelia was swashed and drainage could be placed in. The gastric mucous tissues of the perforation sites of patients in the two groups were collected during the surgery and sent for the pathological examination to confirm their histological characteristics.

2.3. Detection methods for serum indexes

At day 1 after surgery, 4 mL of elbow vein peripheral blood was collected, and serum was separated after centrifuged. ELISA kit was used to detect the contents of interleukin-1β(IL-1β), IL-2, IL-6, IL-8, IL-10, cortisol (Cor), epinephrine (E), norepinephrine (NE), renin (R) and angiotensin-II (Ang-II).

2.4. Evaluation methods for immune function

At day 1 after surgery, 4 mL of fresh blood with heparin anticoagulant was collected and divided into two portions. One portion was centrifuged at 2000 r/min for the bottom red cells, and the density of the red cells was regulated to 1×10^6/mL. Then, 50 μL of red cell suspension was collected and added with 50 μL of sensitized freeze-dried yeast suspension C3b for incubation. Two hundred red blood cell C3bR were counted with oil lens. One more 50 μL of cell suspension was collected and added with 50 μL of non-sensitized freeze-dried yeast suspension for incubation, and then 200 immune complex resette (ICR) were counted with oil lens. Four portions of 50 μL cell suspensions were collected to incubate the fluorescent antibodies of CD58, CD59 and complement receptor 3 (CR3), respectively, and then the average flourescence intensity of CD58, CD59 and CR3 was examined with flow cytometry. The other portion of the fresh blood was used to extract the mononuclear cells of peripheral blood and incubate the fluorescent monoclonal antibodies of CD3, CD4, CD16 and CD56, and then the average flourescence intensity of CD3, CD4, CD16 and CD56 was examined with flow cytometry as well.

2.5. Statistical methods

Software SPSS version 20.0 was used to input and analyze the data. The *t*-test was used to analyze the measurement data between the two groups. Difference was considered as statistically significance when $P < 0.05$.

3. Results

3.1. General information of patients in the two groups

There were 19 patients [(38.46 ± 5.12) years] in the LS group which contained 13 males and 6 females. The perforation time was (6.22 ± 0.97) h, and perforation diameter was (0.52 ± 0.07) cm. In terms of the location of perforation sites, there were 12 cases of

perforation sites at the anterior wall of the gastric antrum, 2 cases at the posterior wall of the gastric antrum, 3 cases at pyloric canal and 2 cases at the lesser curvature. Twenty-five patients with the age of (39.11 ± 5.47) years were divided into the laparotomy group. This group contained 17 males and 8 females. The perforation time was (6.08 ± 0.96) h, and perforation diameter was (0.49 ± 0.06) cm. In terms of the location of perforation sites in this group, there were 16 cases with perforation sites at the anterior wall of the gastric antrum, 2 cases at the posterior wall of the gastric antrum, 4 cases at pyloric canal and 3 cases at the lesser curvature. No significant difference of age, gender, perforation time, perforation diameter and perforation sites between patients in the two groups was observed ($P < 0.05$) (Table 1).

Table 1
Comparison of the general information of patients in the two groups.

Parameter	LS group ($n = 19$)	Laparotomy group ($n = 25$)	P
Age (year)	38.46 ± 5.12	39.11 ± 5.47	> 0.05
Gender (male/female)	13/6	17/8	> 0.05
Perforation time (h)	6.22 ± 0.97	6.08 ± 0.96	> 0.05
Perforation time (h)	0.52 ± 0.07	0.49 ± 0.06	> 0.05
Location of perforation sites			
Anterior wall of the gastric antrum	12	16	> 0.05
Posterior wall of the gastric antrum	2	2	> 0.05
Pyloric canal	3	4	> 0.05
Lesser curvature	2	3	> 0.05

3.2. Degree of patients' inflammatory reaction of both groups

At day 1 after surgery, the contents of serum IL-1β [(4.25 ± 0.52) *vs.* (5.78 ± 0.79) μg/mL], IL-2 [(3.77 ± 0.39) *vs.* (5.18 ± 0.69) μg/mL], IL-6 [(32.69 ± 4.13) *vs.* (43.65 ± 7.58) pg/mL], IL-8 (29.35 ± 2.89) *vs.* (34.13 ± 5.33) pg/mL] and IL-10 [(65.76 ± 7.78) *vs.* (82.15 ± 9.42) pg/mL] of patients in the LS group were significantly lower than those of the laparotomy group. Diffences of the contents of IL-1β, IL-2, IL-6, IL-8 and IL-10 in serum of patients from both groups at day 1 after surgery were considered statistically significant ($P < 0.05$) (Table 2).

Table 2
Comparison of patients' inflammatory reaction indexes of both groups.

Index	LS group ($n = 19$)	Laparotomy group ($n = 25$)	P
IL-1β (μg/mL)	4.25 ± 0.52	5.78 ± 0.79	< 0.05
IL-2 (μg/mL)	3.77 ± 0.39	5.18 ± 0.69	< 0.05
IL-6 (pg/mL)	32.69 ± 4.13	43.65 ± 7.58	< 0.05
IL-8 (pg/mL)	29.35 ± 2.89	34.13 ± 5.33	< 0.05
IL-10 (pg/mL)	65.76 ± 7.78	82.15 ± 9.42	< 0.05

3.3. Degree of patients' stress reaction of both groups

At day 1 after surgery, the contents of Cor [(217.65 ± 22.41) *vs.* (248.69 ± 31.35) ng/mL], NE [(354.31 ± 32.49) *vs.* (464.76 ± 61.34) pg/mL], E (239.63 ± 21.95) *vs.* (278.51 ± 33.59) pg/mL], R [(1.82 ± 0.17) *vs.* (2.29 ± 0.35) ng/mL] and Ang-II [(52.65 ± 5.32) *vs.* (68.98 ± 9.14) pg/mL] in serum of patients in the LS group were significantly lower than those of the laparotomy group. Diffences of the contents of Cor, NE, E, R and Ang-II in serum of patients from both groups at day 1 after surgery showed statistically significance ($P < 0.05$) (Table 3).

Table 3
Comparison of patients' stress reaction indexes of the two groups.

Index	LS Group ($n = 19$)	Laparotomy Group ($n = 25$)	P
Cor (ng/mL)	217.65 ± 22.41	248.69 ± 31.35	< 0.05
NE (pg/mL)	354.31 ± 32.49	464.76 ± 61.34	< 0.05
E (pg/mL)	239.63 ± 21.95	278.51 ± 33.59	< 0.05
R (ng/mL)	1.82 ± 0.17	2.29 ± 0.35	< 0.05
Ang-II (pg/mL)	52.65±5.32	68.98 ± 9.14	< 0.05

3.4. The immune function of patients in the two groups

At day 1 after surgery, the fluorescence intensities of CD3 [(112.32 ± 17.95) *vs.* (82.54 ± 9.35)], CD4 [(47.65 ± 8.16) *vs.* (33.32 ± 4.59)], CD16 [(17.42 ± 3.46) *vs.* (13.42 ± 1.89)] and CD56 [(12.65 ± 2.92) *vs.* (9.14 ± 1.04)] in mononuclear cells of peripheral blood from the LS group were significantly higher than those of the laparotomy group. And the garland number of C3bR [(19.52 ± 4.42) *vs.* (11.38 ± 1.74)] and ICR [(7.42 ± 1.04) *vs.* (4.19 ± 0.56)] in red blood cells, and the fluorescence intensities of CR3 [(58.76 ± 9.35) *vs.* (35.42 ± 4.59)], CD58 [(31.38 ± 6.74) *vs.* (22.76 ± 3.16)] and CD59 [(46.41 ± 9.61) *vs.* (39.15 ± 5.68)] of the LS group were significantly higher than those of the laparotomy group. Differences between the fluorescence intensities of CD3, CD4, CD16, CD56, CR3, CD58, CD59 and the garland number of C3bR and ICR in patients of both groups at day 1 after surgery were considered statistically significant ($P < 0.05$) (Table 4).

Table 4
Comparison of patients' immune function indexes of the two groups.

Index	LS group ($n = 19$)	Laparotomy group ($n = 25$)	P
Conventional immune response			
CD3	112.32 ± 17.95	82.54 ± 9.35	< 0.05
CD4	47.65 ± 8.16	33.32 ± 4.59	< 0.05
CD16	17.42 ± 3.46	13.42 ± 1.89	< 0.05
CD56	12.65 ± 2.92	9.14 ± 1.04	< 0.05
Red cells immune responce			
C3bR	19.52 ± 4.42	11.38 ± 1.74	< 0.05
ICR	7.42 ± 1.04	4.19 ± 0.56	< 0.05
CR3	58.76 ± 9.35	35.42 ± 4.59	< 0.05
CD58	31.38 ± 6.74	22.76 ± 3.16	< 0.05
CD59	46.41 ± 9.61	39.15 ± 5.68	< 0.05

4. Discussion

Emergency treatment with gastric perforation repair surgery is the main surgery method for acute gastric perforation. Laparotomy of gastric perforation repair is widely applied in clinic. However, it causes great surgery trauma and affects the postoperative recovery as well. In recent years, laparoscopic technique has been

significantly developed and widely used for the treatment of general surgical diseases. Gastric perforation repair with laparoscope has the advantages of elaborate operation and little surgery trauma[8-10]. Surgery trauma caused by operation will activate the body's inflammatory reaction leading to a massive synthesis and release of inflammatory mediators. IL is an important inflammatory mediator in body. IL-1β, IL-2, IL-6, IL-8 and IL-10 are closely correlated with the inflammatory reaction caused by the surgery trauma[11,12]. IL-1β and IL-2 are the inflammatory factors mediating inflammatory reaction, which have a direct effect on target tissue and cause inflammatory injury[13]. IL-6 is a multifunctional cytokine which has a regulation effect on inflammatory reaction and immune reponse, and it can also mediate the cascade amplification of inflammatory reaction[14]. IL-8 is the cytokine with an effect of neutrophils chemotaxis, which can improve the activation of neutrophile granulocyte and the release of elastinase during the process of inflammatory reaction[15]. IL-10 is an important anti-inflammatory cytokine in body. The inflammatory reaction caused by surgery trauma will compensatorily increase the secretion of IL-10[16]. It was found by analyzing the contents of the above inflammatory mediators in patients of the two groups that the contents of IL-1β, IL-2, IL-6, IL-8 and IL-10 in serum of patients in the LS group were significantly lower than those of the laparotomy group, which indicated that the inflammatory reaction and the surgery trauma have a quite slight degree after treated with laparoscopic surgery for acute gastric perforation.

Except the inflammatory reaction, stress reaction has also been obviously activated when the body was suffering from surgery trauma. Adrenal gland is an endocrinal organ that plays an important role in the process of stress reaction. E and NE secreted by adrenal medulla and Cor secreted by adrenal cortex are the important endocrine hormones mediating stress reaction[17,18]. When the body is suffering from external trauma, hypothalamicpituitary-adrenal (HPA) axle will be activated and the sympathetic nerve activity is enhanced[19,20]. The activation of HPA axle can improve the synthesis of adrenal cortex and secrete the Cor by adrenocorticotrophic hormone, which can further enhance the capacity to withstand the traumatic stimulus for body by regulating the homeostasis, energy and water sodium metabolism[21]. The enhanced sympathetic nerve activity will improve the release of E and NE, which can further regulate the systole and blood pumping, influence the systaltic condition of peripheral vessel and guarantee the body's blood perfusion of vital organs under stress reaction[22,23]. In the process of stress reaction, except the activation of HPA axle and increased sympathetic nerve activity, renin-angiotensin system will be obviously activated as well. The fluctuation of systemic hemodynamics under stress reaction will activate R with which the angiotensinogen was turned into Ang-I, and then it will be turned into Ang with the catalysis of angiotensin converting enzyme, which will further regulate the systemic blood stream state[24,25]. We can know by analyzing the contents of the above stress hormones in patients of the two groups that the contents of Cor, NE, E, R and Ang-II in patients' serum of the LS group were significantly lowerthan those of the laparotomy group, which indicated that acute gastric perforation treated with laparoscopic surgery showed slight stress reaction and surgery trauma.

The inflammatory reaction and stress reaction caused by surgery trauma will lead to the abnormal secretion of body's hormones and the homeostasis will be destroyed, which will further inhibit the immune response. T lymphocyte and natural killer (NK) cells are important cells mediating the specific immune response and nonspecific immune response of body, respectively. T lymphocyte mainly participates in the process of cellular immune response and simultaneously regulates the humoral immune response by antigen presentation[26,27]. The marker molecule of mature T lymphocyte surface is CD3. The expression level of CD3 in peripheral blood demonstrates the overall number and function of T lymphocyte. CD4 is a surface marker molecule of T-helper cell subpopulation which can participate in the regulation of the immune response by secreting various cytokines[28]. NK cells mediate the cytocidal effect whose surface marker molecules are CD16 and CD56[27,29]. We analyzed the expression levels of marker molecules of surface T lymphocyte and NK cells from mononuclear cells of peripheral blood, and it was found that the fluorescence intensities of CD3, CD4, CD16 and CD56 from mononuclear cells surface of peripheral blood in the LS group were significantly higher than those of the laparotomy group. Immune response in erythrocyte is a new immune response mechanism found in recent years. C3b receptor (CR1) can identify and scavenge the circulating immune complex. Meanwhile, it can enhance the T lymphocyte function through surface molecules of CD58, CD59 and CR3[30,31]. We can know by analyzing the indexes of immune response in erythrocyte, that the fluorescence intensities of CR3, CD58 and CD59 and the garland number of C3bR and ICR of red blood cells in peripheral blood from the LS group were all significantly higher than those of the laparotomy group, which indicated that patients with acute gastric perforation treated by laparoscopic surgery showed slighter inhibition effect on body immune function and more satisfactory postoperative recovery of immune function.

In conclusion, emergency laparoscopic surgery used to treat acute gastric perforation shows slight postoperative inflammatory reaction and stress reaction and presents weak inhibition effect on nonspecific immune response, specific immune response and erythrocyte immune response, which makes less trauma than laparotomy.

Conflict of interest statement

The authors report no conflict of interest.

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