Evaluation of the stress response and immune response after percutaneous transhepatic gallbladder puncture combined with laparoscopic surgery for acute severe cholecystitis

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ABSTRACT

Objective: To study the stress response and immune response after percutaneous transhepatic gallbladder puncture combined with laparoscopic surgery for acute severe cholecystitis.

Methods: A total of 86 patients with severe acute cholecystitis who received surgical treatment in Yulin Second Hospital between April 2013 and April 2017 were selected as the research subjects and randomly divided into two groups, observation group of patients received percutaneous transhepatic gallbladder puncture combined with laparoscopic surgery, control group of patients received emergency laparoscopic surgery, and serum was collected the same day and 3 d after operation to determine the inflammation indexes, stress response indexes and immune response indexes. Results: The same day after operation and 3 d after operation, serum HMGB-1, IL-2, IL-6, hs-CRP, ET-1, ACTH, Cor and MDA levels as well as peripheral blood CD8+ levels of observation group were significantly lower than those of control group while serum SOD, IgG, IgM and IgA levels as well as peripheral blood CD3+ and CD4+ levels were significantly higher than those of control group. Conclusion: Percutaneous transhepatic gallbladder puncture combined with laparoscopic surgery for acute severe cholecystitis can improve the postoperative inflammatory response, stress response and immune response.

1. Introduction

Acute cholecystitis is a common clinical acute abdominal disease, which is characterized by abdominal pain, fever and jaundice. Laparoscopic cholecystectomy is the preferred treatment for it. Severe acute cholecystitis is quite critical, and the local inflammatory exudation is quite obvious, pericholecystic tissue is adhesive, and there is varying degree of systemic inflammatory reaction activation, which greatly increase the difficulty of laparoscopic resection; in addition, the operation trauma will further lead to the cascade activation of the systemic inflammatory response, which is not conducive to the functional recovery of the body and increases the risk of perioperative complications[1,2]. At present, the selection of emergency surgery for acute severe cholecystitis is still controversial and the curative effect of emergency laparoscopic cholecystectomy is not accurate. Percutaneous transhepatic gallbladder puncture is a conservative treatment for acute cholecystitis, it helps reduce inflammatory exudation via biliary drainage, and after local inflammatory response is alleviated, the laparoscopic cholecystectomy can reduce the operation difficulty, and also improve systemic inflammatory response[3-4]. The stress response and immune response after percutaneous transhepatic gallbladder puncture combined with laparoscopic surgery for acute severe cholecystitis were specifically analyzed in the following study.

2. Case information and research methods

2.1 General case information

A total of 86 patients with severe acute cholecystitis who received surgical treatment in Yulin Second Hospital between April 2013 and April 2017 were selected as the research subjects, and all patients had the symptoms of fever and upper abdominal pain as well as the positive Murphy’s signs, were with body temperature > 38 °C and...
2.2 Surgical therapy

Control group received routine treatment such as routine anti-inflammation, spasmylosis, stomach protection and fluid infusion after admission to the hospital, and accepted emergency laparoscopic cholecystectomy after the preoperative examination was completed. Observation group of patients received both conventional support therapy and percutaneous transhepatic gallbladder puncture after admission, which was as follows: ultrasound scan was conducted at first to confirm the location of gallbladder and determine puncture path. 18G puncture needle was used for percutaneous transhepatic gallbladder puncture and bile extraction, guide wire was embedded after confirming the puncture needle was in position, then the puncture needle was withdrawn, then the catheter was inserted into the gallbladder along the guide wire, and drainage bag was connected; after puncture, selective laparoscopic cholecystectomy was performed according to the general condition, and the procedure of laparoscopic cholecystectomy was the same as that of the control group.

2.3 Serum index detection

The same day after operation and 3 d after operation, 5 mL peripheral venous blood was collected from two groups of patients and centrifuged to separate serum, then enzyme-linked immunosorbent assay kit was used to detect HMGB-1, IL-2, IL-6, hs-CRP, ET-1, ACTH, Cor, IgG, IgM and IgA levels, and radioimmunoprecipitation kit was used for determining the contents of SOD and MDA.

2.4 Peripheral blood immune cell detection

The same day after operation and 3 d after operation, peripheral venous blood was collected from two groups of patients to incubate fluorescent antibody CD3, CD4 and CD8 away from light, then the levels of immune cells CD3+, CD4+ and CD8+ were determined in flow cytometer.

2.5 Statistical methods

SPSS 19.0 software was used to input serum and peripheral blood test data, differences in dada between two groups were by t test and \( P<0.05 \) indicated statistical significance in differences in test results.

3. Results

3.1 Postoperative inflammatory response

The same day after operation and 3 d after operation, analysis of serum inflammation indexes HMGB-1 (ng/mL), IL-2 (ng/mL), IL-6 (pg/mL) and hs-CRP (μg/mL) between two groups of patients was as follows: the same day after operation and 3 d after operation, serum HMGB-1, IL-2, IL-6 and hs-CRP levels of observation group were significantly lower than those of control group. Differences in serum HMGB-1, IL-2, IL-6 and hs-CRP levels were statistically significant between two groups of patients the same day after operation and 3 d after operation \( (P<0.05) \).

3.2 Postoperative stress response

The same day after operation and 3 d after operation, analysis of serum stress response indexes ET-1 (pg/mL), ACTH (pmol/L), Cor (nmol/L), SOD (U/mL) and MDA (μmol/mL) between two groups of patients was as follows: the same day after operation and 3 d after operation, serum ET-1, ACTH, Cor and MDA levels of observation group were significantly lower than those of control group while SOD levels were significantly higher than those of control group. Differences in serum ET-1, ACTH, Cor, SOD and MDA levels were statistically significant between two groups of patients the same day after operation and 3 d after operation \( (P<0.05) \).

### Table 1.
Comparison of postoperative inflammation response between two groups of patients.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>HMGB-1</th>
<th>IL-2</th>
<th>IL-6</th>
<th>hs-CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>43</td>
<td>Same day after operation</td>
<td>6.76±0.93</td>
<td>6.48±0.93</td>
<td>54.95±7.82</td>
<td>8.93±1.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 d after operation</td>
<td>4.41±0.56</td>
<td>5.34±0.77</td>
<td>42.46±5.96</td>
<td>7.52±0.88</td>
</tr>
<tr>
<td>Control group</td>
<td>43</td>
<td>Same day after operation</td>
<td>15.25±1.83</td>
<td>9.57±1.15</td>
<td>93.15±11.03</td>
<td>16.48±2.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 d after operation</td>
<td>17.02±2.05</td>
<td>12.31±1.85</td>
<td>120.35±16.85</td>
<td>19.14±2.46</td>
</tr>
</tbody>
</table>

*: comparison between observation group and control group after operation, \( P<0.05 \).

### Table 2.
Comparison of postoperative stress response between two groups of patients.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>ET-1</th>
<th>ACTH</th>
<th>Cor</th>
<th>SOD</th>
<th>MDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>43</td>
<td>Same day after operation</td>
<td>26.62±3.25</td>
<td>3.41±0.49</td>
<td>138.6±16.7</td>
<td>69.7±8.95</td>
<td>6.79±0.93</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 d after operation</td>
<td>21.37±2.58</td>
<td>2.89±0.34</td>
<td>114.5±13.6</td>
<td>76.2±9.35</td>
<td>5.31±0.77</td>
</tr>
<tr>
<td>Control group</td>
<td>43</td>
<td>Same day after operation</td>
<td>38.41±5.28</td>
<td>4.95±0.62</td>
<td>184.2±20.3</td>
<td>50.3±6.72</td>
<td>8.74±0.93</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 d after operation</td>
<td>45.24±6.49</td>
<td>5.73±0.69</td>
<td>215.4±26.7</td>
<td>42.3±5.62</td>
<td>10.35±1.26</td>
</tr>
</tbody>
</table>

*: comparison between observation group and control group after operation, \( P<0.05 \).
occurrence risk of postoperative complications emergency laparoscopic cholecystectomy will on the one hand, the ability of the body to withstand surgical trauma. Therefore, the of inflammatory mediators are released in cascade and attenuate with acute cholecystitis is significantly activated, and a large number removal. In addition, the systemic inflammatory response of patients laparoscopic anatomical structure identification, separation and tight pericholecystic tissue adhesion and increase the difficulty of obvious, and a large amount of inflammatory exudate can cause edema and inflammatory exudation in local gallbladder are acute cholecystitis occurs abruptly and is critical, both hyperemia and other pro-inflammatory factors, the liver cells can synthesize a in the late stage of inflammatory reaction and can promote the cascade amplification of inflammatory response; IL-2 and IL-6 are cytokines with significant pro-inflammatory functions, which promote the inflammatory response activation and infiltration of inflammatory cells and amplify the inflammatory response activation[10,11]; hs-CRP is an acute phase protein synthesized by liver cells, and under the action of IL-2, IL-6 and other pro-inflammatory factors, the liver cells can synthesize a large number of hs-CRP and secrete it into the blood circulation[2]. In the study, comparison of postoperative inflammatory response between two groups of patients showed that the same day after operation and 3 d after operation, serum HMGB-1, IL-2, IL-6 and hs-CRP levels of observation group were significantly lower than those of control group. It means that the inflammatory response after percutaneous transhepatic gallbladder puncture combined with laparoscopic surgery is weaker than that after emergency laparoscopic surgery, suggesting that percutaneous transhepatic gallbladder puncture can reduce the degree of inflammation in patients with severe acute cholecystitis.

The persistent inflammatory response in patients with acute cholecystitis can activate the stress response and cause a variety of acute symptoms and the recovery of functions[8]. In recent years, study has shown the positive efficacy of percutaneous transhepatic gallbladder puncture combined with emergency surgery for severe acute cholecystitis[9], but the change of perioperative inflammatory reaction and immune response is not yet clear. Inflammatory reaction activation is an important characteristic of severe acute cholecystitis, local inflammation activation will increase intraoperative and inflammatory tissue exudation, the activation of systemic inflammatory response can cause the cascade release of a variety of inflammatory mediators, and the levels of inflammatory mediators increase significantly in blood circulation. HMBG1 is a functional protein with strong binding activity, which changes in the study, comparison of postoperative inflammatory response between two groups of patients showed that the same day after operation and 3 d after operation, serum HMGB-1, IL-2, IL-6 and hs-CRP of observation group were significantly lower than those of control group. It means that the inflammatory response after percutaneous transhepatic gallbladder puncture combined with laparoscopic surgery is weaker than that after emergency laparoscopic surgery, suggesting that percutaneous transhepatic gallbladder puncture can reduce the degree of inflammation in patients with severe acute cholecystitis.

3.3 Postoperative immune response status
The same day after operation and 3 d after operation, analysis of peripheral blood immune cells CD3+, CD4+ and CD8+ as well as serum immunoglobulin IgG, IgM and IgA levels between two groups of patients was as follows: the same day after operation and 3 d after operation, peripheral blood CD3+ and CD4+ levels as well as serum IgG, IgM and IgA levels of observation group were significantly higher than those of control group while peripheral blood CD8+ levels were significantly lower than those of control group. Differences in peripheral blood CD3+, CD4+ and CD8+ as well as serum immunoglobulin IgG, IgM and IgA levels were statistically significant between two groups of patients the same day after operation and 3 d after operation ($P<0.05$).

4. Discussion
Laparoscopic cholecystectomy is the preferred therapy for acute cholecystitis, but it is still controversial for the surgery to be used for emergency treatment of acute cholecystitis[5]. Severe acute cholecystitis occurs abruptly and is critical, both hyperemia edema and inflammatory exudation in local gallbladder are obvious, and a large amount of inflammatory exudate can cause tight pericholecystic tissue adhesion and increase the difficulty of laparoscopic anatomical structure identification, separation and removal. In addition, the systemic inflammatory response of patients with acute cholecystitis is significantly activated, and a large number of inflammatory mediators are released in cascade and attenuate the ability of the body to withstand surgical trauma. Therefore, the emergency laparoscopic cholecystectomy will on the one hand, further increase the trauma and lead to the cascade amplification of systemic inflammatory response, and on the other hand, increase the occurrence risk of postoperative complications[6,7]. Percutaneous transhepatic gallbladder puncture is a common emergency conservative therapy for acute cholecystitis, which is used in the elderly patients who cannot tolerate surgery, drains the bile to inhibit local inflammation in local gallbladder, reduce tissue edema and decrease inflammatory exudation, and is helpful for the control of acute symptoms and the recovery of functions[8]. In recent years, study has shown the positive efficacy of percutaneous transhepatic gallbladder puncture combined with emergency surgery for severe acute cholecystitis[9], but the change of perioperative inflammatory reaction and immune response is not yet clear. In the study, comparison of postoperative inflammatory response between two groups of patients showed that the same day after operation and 3 d after operation, serum HMGB-1, IL-2, IL-6 and hs-CRP levels of observation group were significantly lower than those of control group. It means that the inflammatory response after percutaneous transhepatic gallbladder puncture combined with laparoscopic surgery is weaker than that after emergency laparoscopic surgery, suggesting that percutaneous transhepatic gallbladder puncture can reduce the degree of inflammation in patients with severe acute cholecystitis.

The persistent inflammatory response in patients with acute cholecystitis can activate the stress response and cause a variety of active molecules and endocrine hormones to change. ET-1 is a vasoactive substance synthesized by endothelial cells, it has a strong vasoconstriction activity, and the activation of perioperative inflammatory and stress response will increase the synthesis and secretion of endothelial cells ET-1. Cor is the hormone secreted by the adrenal cortex, the secretion of the hormone is regulated by hypothalamus - pituitary - adrenocortical axis (HPA axis), and trauma reactions will increase the HPA axis activation and ATCH
secretion by pituitary gland, which act on the adrenal cortex and promotes the secretion of Cor; Cor has played a variety of biological effects including regulating glucolipid metabolism, sodium excretion and catecholamine sensitivity in the process of stress response[13]. MDA is the lipid oxidation product caused by massive reactive oxygen species secretion in the stress response process, SOD is the antioxidant enzyme with the reactive oxygen species-scavenging effect, and it is massively consumed in the process of stress[14]. In the study, comparison of the postoperative stress reaction between two groups of patients showed that the same day after operation and 3 d after operation, serum ET-1, ACTH, Cor and MDA levels of observation group were significantly lower than those of control group. This means that the stress response after percutaneous transhepatic gallbladder puncture combined with laparoscopic surgery is weaker than that after emergency laparoscopic surgery, suggesting that percutaneous transhepatic gallbladder puncture can reduce the stress response in patients with severe acute cholecystitis. During the activation of postoperative stress response, the immune response process is affected, which is characterized by the inhibition of cellular immune response and humoral immune response. T lymphocyte is one of the important cell mass mediating cellular immune response, CD3 is a marker molecule on mature T cell surface, and when the cellular immune response is restrained, T cell maturation is disabled, and the expression of CD3 reduces significantly. CD4+ and CD8+ are important T-cell subgroups. Under the stress state, the proportion of CD4+ and CD8+ is disturbed, and CD4+ T cell differentiation decreases while CD8+ T cell differentiation increases[15,16]. Immunoglobulin IgG, IgM and IgA are immune active substances synthesized and secreted by plasma cells, which can neutralize pathogen and toxin molecules, and mainly mediate the humoral immune response process. In the study, comparison of the postoperative cellular immune response and humoral immune response between the two groups of patients showed that the same day after operation and 3 d after operation, peripheral blood CD3+ and CD4+ levels as well as serum IgG, IgM and IgA levels of observation group were significantly higher than those of control group while peripheral blood CD8+ levels were significantly lower than those of control group. This means that the inhibition immune response after percutaneous transhepatic gallbladder puncture combined with laparoscopic surgery is weak than that after emergency laparoscopic surgery, suggesting that percutaneous transhepatic gallbladder puncture can improve the immune response in patients with severe acute cholecystitis.

Percutaneous transhepatic gallbladder puncture combined with laparoscopic surgery for severe acute cholecystitis is more effective than emergency laparoscopic surgery in reducing postoperative inflammatory reaction and stress reaction, and improving the cellular immune response and humoral immune response.

References


