Comparison of the degree of inflammatory stress response of laparoscopic myomectomy and abdominal surgery

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ABSTRACT

Objective: To study the degree of inflammatory stress response of laparoscopic myomectomy and abdominal surgery. Methods: Patients who underwent myomectomy in Maternal and Child Health Hospital of Dayi County between June 2014 and October 2017 were retrospectively analyzed, and according to different operation methods, they were divided into the laparoscopy group and the control group who underwent laparoscopic surgery and open surgery respectively. The contents of inflammatory factors and stress mediators in serum as well as the expression of inflammatory molecules and stress molecules in peripheral blood were measured before surgery and 1 d after surgery. Results: Compared with those of same group before surgery, serum TNF-α, sICAM1, sVCAM1, sTREM1, GH, Cor, C-P, FT4 and CRP levels as well as peripheral blood JAK2, STAT3, Notch2, Hes1, Nrf2, HO-1, MPO and FOXP3 expression intensity of both groups of patients were significantly higher after surgery, and serum TNF-α, sICAM1, sVCAM1, sTREM1, GH, Cor, C-P, FT4 and CRP levels as well as peripheral blood JAK2, STAT3, Notch2, Hes1, Nrf2, HO-1, MPO and FOXP3 expression intensity of laparoscopy group of patients after surgery were lower than those of control group. Conclusion: Compared with abdominal surgery, laparoscopic myomectomy can reduce the degree of postoperative inflammatory stress response.

1. Introduction

Uterine fibroid is the most common benign tumor of female reproductive system, its clinical symptom is directly related to the volume and location of uterine fibroids, and small uterine fibroids are mostly without obvious clinical symptoms and need no clinical treatment and intervention; with the increase in the volume of uterine fibroid, there will be abdominal distension and abdominal pain, increased menstrual blood volume, chronic hemorrhagic anemia and other symptoms, and it needs to be treated by myomectomy. Abdominal surgery is the traditional myomectomy, which has large operation space and is easy to operate, but it will inevitably cause major surgical trauma; laparoscopic surgery is the minimally invasive surgery that has been more widely used in gynecological surgery in recent years, which can improve the accuracy and precision of operation, and help to reduce the surgical trauma to the body[1]. About the comparison between laparoscopic myomectomy and abdominal surgery, it has been reported that after laparoscopic surgery, patients’ blood loss is less, time in bed is shorter, and the whole recovery is more ideal[2,3], but there is no report about the differences in inflammation and stress caused by surgical trauma. In the following study, we specifically analyzed the degree of inflammatory stress response after laparoscopic myomectomy.
complete medical history data, the operation was performed by the same group of doctors and postoperative pathology confirmed that the tissue nature was uterine fibroid. A total of 156 patients were included and divided into laparoscopy group and control group according to the different surgical methods of myomectomy. Laparoscopy group (n=72) were operated according to the procedure of laparoscopic myomectomy, they were 39-56 years old and the course of the disease was 3-7 years; control group (n=84) were operated according to the procedure of abdominal myomectomy, they were 37-57 years old, and the course of disease was 3-6 years. There was no significant difference in the general data between the two groups (P>0.05).

2.2. Laboratory detection methods

2.2.1. Serum index detection

Before surgery and 1 d after surgery, 5-6 mL of peripheral venous blood was collected, let stand and then centrifuged in centrifuge for 20 min at the speed of 3 000 r/min to separate serum, and the Elisa kit instructions were followed to determine TNF-α, sICAM1, sVCAM1, sTREM1, GH, Cor, C-P, FT4 and CRP levels.

2.2.2. Peripheral blood molecule detection

Before surgery and 1 d after surgery, another 1-2 mL of peripheral venous blood was collected, anti-coagulated with EDTA at first and then sub-packed to incubate the fluorescent antibody of JAK2, STAT3, Notch2, Hes1, Nrf2, HO-1, MPO and FOXP3 respectively, and finally the molecule expression intensity was measured on flow cytometer.

2.3. Statistical methods

Software SPSS 21.0 was used to input data, the differences in measurement data between groups were analyzed by t test and P<0.05 indicated statistical significance in differences.

3. Results

3.1. Perioperative serum inflammatory factor levels

Before surgery and 1 day after surgery, analysis of serum inflammatory factors TNF-α (ng/mL), sICAM1 (ng/mL), sVCAM1 (ng/mL) and sTREM1 (pg/mL) in the two groups of patients was as follows: compared with the inflammatory factors of same group before surgery, serum TNF-α, sICAM1, sVCAM1 and sTREM1 levels of both groups of patients were significantly higher after surgery (P<0.05); serum TNF-α, sICAM1, sVCAM1 and sTREM1 levels were not significantly different between the two groups of patients before surgery (P>0.05) whereas they were significantly different after surgery (P<0.05), and serum TNF-α, sICAM1, sVCAM1 and sTREM1 levels of laparoscopy group after surgery were lower than those of control group.

3.2. Perioperative peripheral blood inflammatory molecule expression

Before surgery and 1 d after surgery, analysis of peripheral blood inflammatory molecules JAK2, STAT3, Notch2 and Hes1 in the two groups of patients was as follows: compared with the inflammatory molecules of same group before surgery, peripheral blood JAK2, STAT3, Notch2 and Hes1 expression of both groups of patients were significantly higher after surgery (P<0.05); peripheral blood JAK2, STAT3, Notch2 and Hes1 expression were not significantly different between the two groups of patients before surgery (P>0.05) whereas they were significantly different after surgery (P<0.05), and peripheral blood JAK2, STAT3, Notch2 and Hes1 expression of laparoscopy group after surgery were lower than those of control group.

Table 1.
Change trend of perioperative serum inflammatory factors.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>TNF-α</th>
<th>sICAM1</th>
<th>sVCAM1</th>
<th>sTREM1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparoscopy</td>
<td>72</td>
<td>Before surgery</td>
<td>23.1±3.4</td>
<td>214.5±33.6</td>
<td>177.4±22.7</td>
<td>42.6±7.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After surgery</td>
<td>29.8±4.2*</td>
<td>295.1±37.2*</td>
<td>221.6±29.4*</td>
<td>56.1±7.7*</td>
</tr>
<tr>
<td>Control group</td>
<td>83</td>
<td>Before surgery</td>
<td>22.7±3.7</td>
<td>216.2±29.5</td>
<td>179.1±23.1</td>
<td>43.1±6.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After surgery</td>
<td>45.1±6.2</td>
<td>384.6±51.3*</td>
<td>279.3±32.6*</td>
<td>82.5±10.3*</td>
</tr>
</tbody>
</table>

*: Comparison between before and after surgery within group, P<0.05; #: comparison between groups after surgery, P<0.05.

Table 2.
Change trend of perioperative peripheral blood inflammatory molecules.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>JAK2</th>
<th>STAT3</th>
<th>Notch2</th>
<th>Hes1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparoscopy</td>
<td>72</td>
<td>Before surgery</td>
<td>1.02±0.13</td>
<td>1.01±0.15</td>
<td>0.97±0.14</td>
<td>1.03±0.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After surgery</td>
<td>1.55±0.22*</td>
<td>1.41±0.18*</td>
<td>1.62±0.20*</td>
<td>1.36±0.18*</td>
</tr>
<tr>
<td>Control group</td>
<td>83</td>
<td>Before surgery</td>
<td>1.01±0.14</td>
<td>0.99±0.12</td>
<td>1.02±0.15</td>
<td>1.02±0.14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After surgery</td>
<td>2.24±0.35*</td>
<td>2.78±0.41*</td>
<td>2.19±0.35*</td>
<td>1.89±0.22*</td>
</tr>
</tbody>
</table>

*: Comparison between before and after surgery within group, P<0.05; #: comparison between groups after surgery, P<0.05.
Change trend of perioperative peripheral blood stress mediators.

### Table 3.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>GH</th>
<th>Cor</th>
<th>C-P</th>
<th>FT4</th>
<th>CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparoscopy group</td>
<td>72</td>
<td>Before surgery</td>
<td>127.3±15.7</td>
<td>183.9±22.3</td>
<td>1.15±0.15</td>
<td>13.5±2.1</td>
<td>2.94±0.34</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After surgery</td>
<td>164.1±22.3*</td>
<td>211.2±24.6*</td>
<td>1.67±0.22*</td>
<td>16.8±2.4*</td>
<td>3.78±0.51*</td>
</tr>
<tr>
<td>Control group</td>
<td>83</td>
<td>Before surgery</td>
<td>128.1±14.8</td>
<td>184.5±21.8</td>
<td>1.12±0.13</td>
<td>13.2±1.9</td>
<td>2.89±0.37</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After surgery</td>
<td>203.5±29.3</td>
<td>240.3±29.3</td>
<td>2.21±0.34</td>
<td>23.2±2.1</td>
<td>5.61±0.78</td>
</tr>
</tbody>
</table>

*: Comparison between before and after surgery within group, \( P < 0.05 \); *#: comparison between groups after surgery, \( P < 0.05 \).

### Table 4.

Change trend of perioperative peripheral blood stress molecules.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>Nrf2</th>
<th>HO-1</th>
<th>MPO</th>
<th>FOXP3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparoscopy group</td>
<td>72</td>
<td>Before surgery</td>
<td>1.04±0.15</td>
<td>1.01±0.15</td>
<td>1.02±0.17</td>
<td>0.98±0.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After surgery</td>
<td>1.45±0.22*</td>
<td>1.49±0.24*</td>
<td>1.57±0.26*</td>
<td>1.62±0.27*</td>
</tr>
<tr>
<td>Control group</td>
<td>83</td>
<td>Before surgery</td>
<td>1.02±0.12</td>
<td>1.03±0.16</td>
<td>1.01±0.14</td>
<td>1.02±0.14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After surgery</td>
<td>1.93±0.25*</td>
<td>2.25±0.34*</td>
<td>2.41±0.36*</td>
<td>2.56±0.39*</td>
</tr>
</tbody>
</table>

*: Comparison between before and after surgery within group, \( P < 0.05 \); *#: comparison between groups after surgery, \( P < 0.05 \).

3.3. Perioperative serum stress mediator levels

Before surgery and 1 day after surgery, analysis of serum stress mediators GH (pmol/L), Cor (ng/mL), C-P (ng/mL), FT4 (pmol/L) and CRP (mg/L) in the two groups of patients was as follows: compared with the stress mediators of same group before surgery, serum GH, Cor, C-P, FT4 and CRP levels of both groups of patients were significantly higher after surgery \( (P<0.05) \); serum GH, Cor, C-P, FT4 and CRP levels were not significantly different between the two groups of patients before surgery \( (P>0.05) \) whereas they were significantly different after surgery \( (P<0.05) \), and serum GH, Cor, C-P, FT4 and CRP levels of laparoscopy group after surgery were lower than those of control group.

3.4. Perioperative peripheral blood stress molecule expression

Before surgery and 1 day after surgery, analysis of peripheral blood stress molecules in the two groups of patients was as follows: compared with the stress molecules of same group before surgery, peripheral blood Nrf2, HO-1, MPO and FOXP3 expression of both groups of patients were significantly higher after surgery \( (P<0.05) \); peripheral blood Nrf2, HO-1, MPO and FOXP3 expression were not significantly different between the two groups of patients before surgery \( (P>0.05) \) whereas they were significantly different after surgery \( (P<0.05) \), and peripheral blood Nrf2, HO-1, MPO and FOXP3 expression of laparoscopy group after surgery were lower than those of control group.

4. Discussion

The minimal invasiveness of laparoscopic myomectomy has been widely confirmed, but there is no report about changes in the internal environment caused by trauma. The activation of inflammatory response is one of the characteristics of the internal environment changes in the body after the operation, and a variety of inflammatory cytokines are massively synthesized and secreted in the process. TNF- \( \alpha \) is a cytokine with pro-inflammatory activity, which is massively secreted in the initial stage of inflammatory reaction, and participates in the cascade amplification process of inflammatory response[4]; sICAM1 and sVCAM1 are the soluble forms of adhesion factors ICAM1 and VCAM1, which mediate the adhesion and migration of various inflammatory cells, facilitate the infiltration of inflammatory cells in inflammatory sites and participate in the amplification of inflammatory response[5]; sTREM1 is a cytokine that triggers inflammation and participates in the initiation of inflammatory response. In the study, analysis of the perioperative changes in above inflammatory factors showed that compared with the inflammatory factors of same group before surgery, serum TNF- \( \alpha \), sICAM1, sVCAM1 and sTREM1 levels of both groups of patients were increasing after surgery, and serum TNF- \( \alpha \), sICAM1, sVCAM1 and sTREM1 levels of laparoscopy group after surgery were lower than those of control group. This means that the inflammatory response in the body has been activated to different degrees after laparoscopic surgery and abdominal surgery, and the activation of inflammatory response after laparoscopic surgery is weaker than that after abdominal surgery, which indicates that the trauma degree of laparoscopic surgery is weaker than that of abdominal surgery.

The activation of inflammatory response by surgical trauma is dependent on the signal transduction of multiple inflammatory pathways in the body, and the JAK2/STAT3 and Notch2/Hes1 are the two inflammatory pathways known at present. JAK2 and STAT3 family members, which are activated in the signal transduction of multiple inflammatory pathways in the body, and the JAK2/STAT3 and Notch2/Hes1 pathways depend on the signal transduction of multiple inflammatory pathways after laparoscopic surgery is weaker than that after abdominal surgery, which indicates that the trauma degree of laparoscopic surgery is weaker than that of abdominal surgery.
Surgical trauma is a strong stressor for the body, which will cause the excessive activation of stress response and be accompanied by the changes in the levels of various endocrine hormones[8]. The hypothalamus-pituitary-adrenal cortex axis is the target endocrine gland axis that plays an important role in the process of stress reaction, and adrenal cortex secretes a lot of Cor under the action of pituitary hormone ACTH and can enhance the ability of the body to tolerate stress[9]; at the same time, the stimulation of the pituitary gland will also increase the pulsatile secretion of GH and enhance the body’s metabolic rate[10]. Both Cor and GH are endocrine hormones with glycemic effect, and the irritable elevation of blood glucose can stimulate the secretion of insulin and the production of by-product C-P. In addition to the hypothalamus and adrenal cortex that participate in the process of stress, the FT4 secreted by the thyroid and the CRP secreted by the liver are also closely associated with stress, the former can enhance the body’s metabolic rate, and the latter belongs to the acute phase proteins.

Both groups of patients were increasing after surgery, and serum GH, Cor, C-P, FT4 and CRP levels of both groups of patients were lower than those of control group. It indicates that the stress response in the body has been activated to different degrees after laparoscopic surgery and abdominal surgery, and the activation of stress response after laparoscopic surgery is weaker than that after abdominal surgery, which also indicates that the trauma degree of laparoscopic surgery is weaker than that of abdominal surgery.

The activation of postoperative stress response not only involves the changes in endocrine hormones, but will also cause the abnormal activation of various signaling molecules. Nrf2 is the signaling molecule involved in the anti-oxidation process, and the excessively activated stress response can cause Nrf2 activation, start the expression of HO-1 through downstream ARE, and then exert antioxidant activity through HO-1[12,13]; MPO is a molecule expressed by activated neutrophil, which can mediate the generation of reactive oxygen and aggravate the oxidative stress response in the body[14]; FOXP3 is a type of immune cell transcription factor, and the immune suppression caused by stress response is related to the up-regulation of FOXP3 expression[15]. In the study, we further analyzed the perioperative changes in above stress mediators showed that compared with the stress mediators of same group before surgery, serum GH, Cor, C-P, FT4 and CRP levels of both groups of patients were increasing after surgery, and serum GH, Cor, C-P, FT4 and CRP levels of laparoscopy group after surgery were lower than those of control group. It indicates that the stress response in the body have been activated to different degrees after laparoscopic surgery and abdominal surgery, and the activation of stress response after laparoscopic surgery is weaker than that after abdominal surgery, which also indicates that the trauma degree of laparoscopic surgery is weaker than that of abdominal surgery.

Above all, it can be concluded that compared with abdominal surgery, laparoscopic myomectomy can reduce the activation of postoperative inflammatory stress reaction, reduce the release of inflammatory factors and stress hormones, and also inhibit the activation of corresponding signaling pathways.

References