Clinical effects of laparoscopic surgery on treating ovarian benign tumor and influences of it on serum reproductive hormones, inflammatory factors, immune function and neuroendocrine hormones levels in patients

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ABSTRACT

Objective: To investigate clinical effects of laparoscopic surgery on treating ovarian benign tumor and explicit influences of it on serum reproductive hormones, inflammatory factors, immune functions and neuroendocrine hormone levels in postoperative patients. Methods: A total of 116 cases of patients with ovarian benign tumor were selected and randomly divided as 58 cases of the control group and the observation group. For control group, open surgery therapy was provided, for observation group, laparoscopic surgery therapy was given. Situation of these two therapeutic operations and variations of serum reproductive hormones (E\(_2\), FSH, LH), inflammatory factors (CRP, TNF-\(\alpha\), IL-6), immune functions (CD3\(^+\), CD4\(^+\), CD8\(^+\), CD4\(^+\)/CD8\(^+\)), neuroendocrine hormones (COR, \(\beta\)-endorphin, glucagon) levels were compared.

Results: After operation, E\(_2\) levels in observation group were significantly lower than control group, FSH, LH were significantly higher than control group, differences between the two groups were significant. Biochemical indexes on 1 d, 3 d after operation and CRP, TNF-\(\alpha\), IL-6, CD8\(^+\), COR, \(\beta\)-endorphin, glucagon levels in observation group were lower than control group, significant differences showed between groups; CD3\(^+\), CD4\(^+\), CD4\(^+\)/CD8\(^+\) levels in observation group were significantly increased comparing with control group, differences were significant with statistical significance. Conclusion: Effects of laparoscopic surgery on treating ovarian benign tumor were significant. The surgery could effectively improve ovarian functions for patients with less damage on body immune system, it could effectively diminish suppression of immune function and release stress response.

1. Introduction

Ovarian tumor is a common gynecological tumor on clinic. Mainly of ovarian tumors were benign. Surgery treatment is a preferred therapeutic method. Currently, more clinical applied surgeries are open and laparoscopic surgeries, especially the laparoscopic surgery. Because of its advantages, such as minimally invasive, rapid recovery, it has been widely used on diagnosis and treatment for gynecologic diseases\(^{[1,2]}\). Researches verified that surgery was a trauma stress for patients' bodies. It had significant influences on biochemical indexes, such as immune functions, neuroendocrine hormones levels and prognosis on patients\(^{[3]}\). Our research aims to observe therapeutic effects of laparoscopic surgery on treating ovarian benign tumor and influences of it on biochemical indexes, such as serum reproductive hormones, inflammatory factors, immune functions and neuroendocrine hormone levels in postoperative patients, thus to make sure function details of laparoscopic surgery on treating ovarian benign tumors, and provide references for clinical applications.

2. Materials and methods

2.1. General materials
A total of 116 cases of patients with ovarian benign tumor treated in our hospital from Apr 2014 to Oct 2016 were selected as subjects. Diseases of all the patients were diagnosed by routine ultrasound examination and tumor markers detection[4]. Ages were ranged from 28 to 59 years old. Patients were randomly divided as the control group and observation group, 58 cases each. Difference of age composition in two groups of patients were not significant (P>0.05), which were comparable. Our research had been approved by ethic committee in our hospital, and informed consents were received from patients.

2.2. Selected and excluded standards

Select standards: (1) Clinical behaviors, ultrasound CT/MRI and prognosis pathologies in all the patients were verified disease as ovarian benign tumors; (2) All the patients had surgery indications, and had no absolute surgery contraindications; (3) Patients all volunteered into this research. And they all had complete materials.

Excluded standards: (1) Patients combinations who had severe cardiovascular and cerebrovascular diseases, liver and renal dysfunctions and other genital system diseases; (2) Patients combinations who had severe immune dysfunctions and endocrine disorder; (3) Patients who had been administered glucocorticoid medications or immune suppressors within one month before treatment; (4) Patients combinations who had trend of infectious bleeding[5].

2.3. Surgery methods

Control group: Treatments of routine open surgeries were utilized. Combined spinal and epidural analgesia was given on patients. And ovarian cystectomy via ventral midline incision was processed.

Observation group: Therapeutic projects of laparoscopic surgery were utilized. General anesthesia or continuous epidural plus intravenous anesthesia were processed on patients. Standard three holes operational approach was used. Cyst puncture sectional decollement or complete cyst excision surgery (adnexectomy) was utilized for treatment. Routine preventive infectious treatments were processed in two groups of patients after surgeries.

2.4. Observation indexes and detective methods

2.4.1. Observation indexes

Clinical effects and influences on inflammatory factors levels, immune function and neuroendocrine hormones levels between two groups of patients were observed and compared. Serum reproductive hormones levels, like Estradiol (E2), follicle-stimulating hormone (FSH) and luteinizing hormone (LH), were detected to reflect ovarian recovery condition (clinical effects).

The inflammatory factors included C-reaction protein (CRP), tumor necrosis factor (TNF-α) and interleukin (IL-6); Immune function indexes were T lymphocyte subsets CD3+, CD4+, CD8+, CD4+/CD8+; Neuroendocrine hormones included cortisol (COR), β-endorphin and glucagon.

2.4.2. Detective methods

For all the patients, serum reproductive hormones levels (E2, FSH, LH) before and 3rd day after surgeries were detected. On 1st day and 3rd day, inflammatory factors, immune function and neuroendocrine hormones levels were detected, inflammatory factors (CRP, TNF-α, IL-6) and β-endorphin were detected by ELISA method. The kits were provided by Beijing Jingmei Biological Engineering Co., Ltd; T lymphocyte subsets were CD3+, CD4+, CD8+, CD4+/CD8+ levels were detected by CoulterEpics-XL flow cytometry (manufacturer: Beckman Coulter Inc. USA); Glucagon and COR were detected by radioimmunoassay.

2.5. Statistical methods

SPSS 17.0 statistical software was used for analyzing data of results. The quantitative data were indicated by average number ± standard derivation (Mean ± SD). Comparison of samples average numbers were measured by independent sample t. Comparison of enumeration data were analyzed by chi square. P<0.05 showed that differences had statistical significance.

3. Results

3.1. Comparison of serum reproductive hormones levels in two groups of patients before and after surgeries

Comparison results of serum reproductive hormones levels in two groups of patients before and 3rd day after surgeries were showed in below Table 1. No significant difference showed comparing with E2, FSH, LH levels before surgeries between two groups of patients (P>0.05). After surgeries, E2 levels in two groups of patients were significantly decreased comparing with the same groups before surgeries. The differences were obvious. They had statistical significance (P<0.05).

And levels in observation group were significantly lower than control group, the differences were obvious with statistical significance (P<0.05). FSH and LH levels in two groups after surgeries were significantly increased comparing with the same groups before surgeries, the differences were obvious with statistical significance (P<0.05). Levels in observation group after surgery were (18.67±1.61) U/L and (14.93±1.30) U/L, which were significantly higher than levels (13.09±1.84) U/L and (10.73±1.17) U/L in control group, the differences between groups were obvious with statistical significance (P<0.05).

3.2. Comparison of inflammatory factor levels in two groups of patients before and after surgeries

Variation of inflammatory factors levels before and on 1st day and 3rd day after surgeries were showed in Table 2. Comparison of CRP, TNF-α, IL-6 indexes levels showed that the differences were not obvious, and no statistical significance (P>0.05). The three
Comparison of CD3 of patients before and after surgeries were showed in Table 3. Variation of immune function related indexes levels in two groups before and after surgeries.

3.3. Comparison of immune function related indexes in two groups of patients before and after surgeries.

Variation of immune function related indexes in two groups of patients before and after surgeries were showed in Table 3. Comparison of CD3\(^+\), CD4\(^+\), CD8\(^+\), CD4\(^+\)/CD8\(^+\) levels between two groups of patients before surgeries showed no statistical significant difference (P>0.05). Within the same group, CD3\(^+\), CD4\(^+\) levels in two groups on 1st day and 3rd day after surgery were significantly decreased comparing with levels before surgeries, differences were obvious with statistical significance (P<0.05), and levels on 3rd day of surgeries were significantly higher than on 1st day after surgeries, differences were obvious with statistical significance (P<0.05); CD8\(^+\) levels on 1st day after surgery were significantly increased comparing with which before surgeries, and levels on 3rd day after surgeries were significantly decreased comparing with which on 1st day after surgeries, differences between two groups were obvious with statistical significance (P<0.05); CD4\(^+\)/CD8\(^+\) levels within the same group showed that in two groups of patients, levels on 1st day after surgeries were significantly decreased comparing with which before surgeries and 1st day after surgeries, differences between two groups were obvious with statistical significance (P<0.05). Variation results of neuroendocrine hormones levels in two groups of patients before and after surgeries were showed in Table 4. Variation results of neuroendocrine hormones levels in two groups of patients before and after surgeries showed no obvious difference, no statistical significance existed (P>0.05). Within the same group, COR, \(\beta\)-endorphin and glucagon levels within the same phase were significantly higher than control group at the same phase, while CD8\(^+\) levels were significantly decreased comparing with the same phase in control group (P<0.05).

### Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>E(_2) (nmol/L)</th>
<th>FSH (U/L)</th>
<th>LH (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Before surgery</td>
<td>71.42±3.73</td>
<td>7.39±1.14</td>
<td>6.67±1.09</td>
</tr>
<tr>
<td></td>
<td>After surgery</td>
<td>66.81±3.46</td>
<td>13.09±1.84</td>
<td>10.73±1.17</td>
</tr>
<tr>
<td>Observation</td>
<td>Before surgery</td>
<td>71.58±4.51</td>
<td>7.41±1.22</td>
<td>6.88±1.21</td>
</tr>
<tr>
<td></td>
<td>After surgery</td>
<td>62.09±3.10(^a)</td>
<td>18.67±1.61(^b)</td>
<td>14.93±1.30(^c)</td>
</tr>
</tbody>
</table>

\(^a\) indicated that compared with the same group before treatment, P<0.05; \(^b\) indicated that compared with control group, P<0.05.

### Table 2

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>CRP (mg/L)</th>
<th>TNF-(\alpha) (ng/L)</th>
<th>IL-6 (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Before surgery</td>
<td>8.59±3.76</td>
<td>12.36±3.14</td>
<td>8.52±3.01</td>
</tr>
<tr>
<td></td>
<td>1st day after surgery</td>
<td>34.25±6.47(^a)</td>
<td>30.28±5.71(^b)</td>
<td>59.87±12.11(^*)</td>
</tr>
<tr>
<td></td>
<td>3rd day after surgery</td>
<td>22.31±6.95(^ab)</td>
<td>20.87±5.18(^b)</td>
<td>34.85±11.71(^b)</td>
</tr>
<tr>
<td>Observation</td>
<td>Before surgery</td>
<td>8.53±3.52</td>
<td>12.38±3.47</td>
<td>8.49±3.04</td>
</tr>
<tr>
<td></td>
<td>1st day after surgery</td>
<td>24.71±7.31(^a)</td>
<td>19.74±4.42(^c)</td>
<td>43.97±10.81(^a)</td>
</tr>
<tr>
<td></td>
<td>3rd day after surgery</td>
<td>9.77±3.71(^ac)</td>
<td>13.62±4.09(^b)</td>
<td>9.82±4.49(^*)</td>
</tr>
</tbody>
</table>

\(^a\) indicated that compared with the same group before treatment, P<0.05; \(^b\) indicated that compared with control group, P<0.05.

### Table 3

Comparison of immune function related indexes in two groups of patients before and after surgeries (n=58).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>CD3(^+) (%)</th>
<th>CD4(^+) (%)</th>
<th>CD8(^+) (%)</th>
<th>CD4(^+)/CD8(^+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Before surgery</td>
<td>63.28±6.41</td>
<td>43.25±5.84</td>
<td>32.49±3.14</td>
<td>1.30±0.22</td>
</tr>
<tr>
<td></td>
<td>1st day after surgery</td>
<td>50.89±6.57(^ab)</td>
<td>28.64±4.42(^ab)</td>
<td>35.22±4.41(^ab)</td>
<td>1.16±0.18(^b)</td>
</tr>
<tr>
<td></td>
<td>3rd day after surgery</td>
<td>57.81±5.49(^bc)</td>
<td>33.41±5.29(^abc)</td>
<td>31.26±3.39(^bc)</td>
<td>1.39±0.21(^b)</td>
</tr>
<tr>
<td>Observation</td>
<td>Before surgery</td>
<td>63.65±6.19</td>
<td>43.41±5.57</td>
<td>32.57±6.27</td>
<td>1.33±0.20</td>
</tr>
<tr>
<td></td>
<td>1st day after surgery</td>
<td>56.37±5.83(^abc)</td>
<td>32.67±5.88(^abc)</td>
<td>33.63±4.17(^ab)</td>
<td>1.25±0.21(^b)</td>
</tr>
<tr>
<td></td>
<td>3rd day after surgery</td>
<td>61.28±4.49(^abc)</td>
<td>39.83±5.27(^abc)</td>
<td>30.13±2.61(^ab)</td>
<td>1.47±0.22(^abc)</td>
</tr>
</tbody>
</table>

\(^a\) indicated that compared with the same group before treatment, P<0.05; \(^b\) indicated that compared with the same group on 1st day after surgery, P<0.05; \(^c\) indicated that compared with control group at the same phase, P<0.05.
on 1st day and 3rd day after surgeries were significantly increased comparing with which before surgeries, the differences were obvious with statistical significance \((P<0.05)\). These three levels on 3rd day after surgeries were significantly lower than which on 1st day after surgeries, differences were obvious with statistical significance \((P<0.05)\); Comparison of levels between observation group and control group showed that levels in observation group on 1st day and 3rd day after surgery were significantly decreased comparing with control group at the same phase. Differences between two groups were obvious with statistical significance \((P<0.05)\).

4. Discussion

Benign ovarian tumor is a common gynecological tumor. Its traditional method for clinical therapy is open surgery therapy. However, the surgery could made more damage on patients bodies, and it could generate relatively high stress reactions. The recovery duration after surgery is long. And bleeding amount during the surgery is more. Patients could have various degrees of immune functional suppression, neuroendocrine hormones imbalance and other adverse reactions, which could seriously threaten safety and prognosis of patients in perioperative period[6]. Laparoscopic surgery has some characteristics on clinic, such as small trauma, fast recovery after surgery and significant clinical effects. It was considered as an effective method for treating ovarian benign tumor[7,8]. Our research aimed to discuss clinical effects of laparoscopic and open surgeries on treating ovarian benign tumor, and to make sure variations of inflammatory factors, immune function and neuroendocrine hormones levels on patients before and after surgeries.

As a defensive structure, immune system plays important roles in courses of body anti-infection, antineoplastic and postoperative recovery. When inflammation, infection, tumor or tissue damage appears, self-immune system could be activated. It could generate and release large amount of TNF-α inflammatory factors. TNF-α could function with multiple cells and excite IL-6 activity, induce cascade reaction, lead to appearance of body inflammatory reactions, thus to make cell and tissue damage. IL-6 is produced by multiple kinds of lymphocytic (non-lymphocytic) cells in spontaneous or stimulation. Its activity has duality. On one hand it could promote proliferation and differentiation of T, B cells and secret antibodies to strengthen body immune function. On the other hand, it could be involved in body inflammatory reactions and pathological process. Its serum levels have close correlation with appearance and progression of pathology. In addition, as a major cytokine inducing synthesis of liver cells, it could induce generation and secretion of CRP. CRP is an important acute reactive protein. Its serum levels have positive correlation with surgery damage degrees. Serum CRP levels could increase during 4–12 h after surgeries, and arrive to a high peak in 48–72 h duration[10]. Some researches indicated that serum CRP and IL-6 levels after surgery had positive correlation with the damage degree of surgery. The two levels could be early sensitive indexes to reflect tissue damage[11]. In our research, comparison results of inflammatory factors levels in two groups of patients indicated that CRP, TNF-α, IL-6 levels on 1st day after surgeries were significantly increased comparing with which before surgeries. And each index levels were significantly decreased on 3rd day after surgeries. For patients with open surgery, CRP, TNF- α, IL-6 levels were still significantly higher than which before surgery.

Levels in patients with laparoscopic surgery had been already recovered to be levels before surgery. Results were consistent with which in previous reports[12,13], which indicated that laparoscopic surgery therapy had less damage on humoral immune system than open surgery therapy, which could effectively diminish infectious complications after surgeries.

Extensive research found that some biochemical indexes, such as immune function and neuroendocrine hormones levels, were sensitive to variation of inner environment, which could be evaluation indexes to judge appearances of adverse reactions during surgeries and after surgeries. Among them, immune functional evaluation indexes mainly were T lymphocytes. Researches have found that levels of T lymphocytic subsets had important clinical significance on disease progression in perioperative period and prognosis recovery of patients[14,15]. In recent years, relevant domestic researches indicated that surgery therapy for elders with ovarian tumor had some suppressive function on immune function of patients, the indexes levels showed decline of CD3⁺, CD4⁺ and CD4⁺/CD8⁺ levels and increase of CD8⁺ levels[6]. Results of our research showed that CD3⁺, CD4⁺ and CD4⁺/CD8⁺ levels in two groups of patients on 1st day after surgeries were significantly decreased comparing with the levels before surgeries, CD8⁺ levels were significantly increased comparing with which before surgeries. On 3rd day after surgeries, CD3⁺, CD4⁺ and CD4⁺/CD8⁺ levels picked up, CD8⁺ levels were decreased. For patients with laparoscopic surgery, CD3⁺, CD4⁺ and CD4⁺/CD8⁺ levels on 1st and 3rd day after surgery were higher than levels in patients with open surgery therapy at the same phase, and CD8⁺ levels were lower than levels in patients with open surgery therapy at the same phase. The

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**Table 4**

Comparison of neuroendocrine hormones levels in two groups of patients before and after surgeries \((n=58)\).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>COR (nmol/L)</th>
<th>β-Endorphin (pg/mL)</th>
<th>Glucagon (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Before surgery</td>
<td>140.3±12.79</td>
<td>141.32±20.59</td>
<td>341.29±25.61</td>
</tr>
<tr>
<td></td>
<td>1st day after surgery</td>
<td>213.68±18.99</td>
<td>174.72±22.03</td>
<td>375.28±25.45</td>
</tr>
<tr>
<td></td>
<td>3rd day after surgery</td>
<td>170.71±13.43</td>
<td>162.66±20.35</td>
<td>342.57±21.49</td>
</tr>
<tr>
<td>Observation</td>
<td>Before surgery</td>
<td>139.87±12.62</td>
<td>141.19±21.05</td>
<td>312.06±21.87</td>
</tr>
<tr>
<td></td>
<td>1st day after surgery</td>
<td>177.85±16.63</td>
<td>158.41±20.99</td>
<td>339.48±23.89</td>
</tr>
<tr>
<td></td>
<td>3rd day after surgery</td>
<td>151.74±12.55</td>
<td>149.47±21.29</td>
<td>322.57±28.23</td>
</tr>
</tbody>
</table>

* a indicated that compared with the same group before treatment, \(P<0.05\); * b indicated that compared with the same group on 1st day after surgery, \(P<0.05\); * c indicated that compared with control group at the same phase, \(P<0.05\).
differences were obvious with statistical significance (P<0.05). The results of our research were consistent with which in reports wrote by Xiao et al.[17,18], which further verified the recoverable suppress function of surgery therapy on patients with ovarian tumors, and laparoscopic surgery therapy had a lower degree of suppression on immune function of patients, which could be more beneficial on recovery of immune function.

Furthermore, researches verified that when intense stimulation outside were received, bodies could generate corresponding reflected stress reactions, which could show up as a rapid increase of neuroendocrine hormones levels, the increased levels had positive correlation with strength of stress reactions[19]. Researches found that when serum COR and β-endorphin levels were in a relatively stable condition, the incident rates of adverse reactions and complications of patients in perioperative period were relatively lower[20]. Relevant results in our research showed that serum COR, β-endorphin and glucagon levels of patients on 1st day after surgeries were significantly increased comparing with which before surgeries. Then on 3rd day after surgeries, each index levels were significantly decreased. And levels of patients with laparoscopic surgery therapy were significantly lower than levels of patients with traditional open surgery therapy. Results indicated that bodies had some self-regulating functions on neuroendocrine systems. And laparoscopic surgery therapy had less influence on neuroendocrine hormones levels after surgery than open surgery therapy, which were consistent with previous reports[21-23], and further revealed that laparoscopic surgery therapy could help to release stress reactions on patients with ovarian benign tumor in perioperative period.

Above all, laparoscopic surgery therapy for ovarian benign tumor could effectively improve ovarian functions of patients. It has significant clinical effects, less damage on body immune system. It could diminish suppression of surgeries on immune function and relieve stress reactions in laparoscopic surgery therapy. It has important clinical value on recovery or others after surgery on patients.

References