Effects of dezocine combined with anesthesia on serum GSH, CAT, MDA, SOD, TNF-α, CRP, IL-6 and T lymphocyte subsets in patients after laparoscopic surgery for colon cancer

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ABSTRACT

Objective: To study the effects of dezocine combined with anesthesia on serum GSH, CAT, MDA, SOD, TNF-α, CRP, IL-6 and T lymphocyte subsets in patients after laparoscopic surgery for colon cancer. Methods: A total of 120 patients with laparoscopic cholecystectomy in our hospital from January 2014 to January 2017 were enrolled in this study. The patients were divided into the control group (n=60) and the treatment group (n=60) randomly. The control group were treated with remifentanil combined anesthesia while the treatment group were treated with dezocine combined with anesthesia. The serum GSH, CAT, MDA, SOD, TNF-α, CRP, IL-6 and peripheral blood CD3+, CD4+, CD8+, CD4+/CD8+ of the two groups before and after surgery were compared. Results: There were no significantly differences of the serum GSH, CAT, MDA, SOD of the two groups before surgery. The serum GSH, CAT, and SOD of the two groups after surgery were significantly lower than those before surgery, the serum MDA of the two groups after surgery were significantly higher than before surgery, and the serum MDA of the treatment group after surgery were significantly better than that of the control group. There were no significantly differences of the serum TNF-α, CRP, IL-6 of the two groups before surgery. The serum TNF-α, CRP, and IL-6 of the two groups after surgery were significantly higher than those before surgery, and these indexes of the treatment group after surgery were significantly lower than those of the control group. Conclusions: Dezocine combined with anesthesia can reduce the oxidative stress reaction in patients after laparoscopic surgery for colon cancer, lower serum TNF-α, CRP, IL-6 levels, and has smaller effect on cellular immune function. Therefore, it is worthy of clinical application.

1. Introduction

Colon cancer is a common malignant tumor in digestive department. Its location is located at the junction of rectum and sigmoid colon. It has high morbidity and mortality in China, whose incidence and fatality rate are in the forefront of malignant tumors[1,2]. At present, laparoscopic surgery is the most important treatment for colon cancer. It has the advantages of small trauma, good safety and less complications. However, because it is still invasive treatment, surgical operation, intraoperative anesthesia and pain stimulation will cause perioperative stress reaction, leading to local oxidative damage and inflammatory response, which will affect the prognosis and prognosis[3,4]. Studies have shown that the stress response in anesthesia and laparoscopic surgery are closely related[5]. Dezocine is a mixed opioid receptor agonist antagonist
and has analgesic effect with morphine, which can inhibit the excessive release of inflammatory mediators and inflammatory factors to reduce tissue damage [6]. This study was to investigate the effects of dezocine combined with anesthesia on serum GSH, CAT, MDA, SOD, TNF-α, CRP, IL-6 and T lymphocyte subsets in patients after laparoscopic surgery for colon cancer. The results of the study are as follows.

2. Materials and methods

2.1. General information

A total of 120 patients who were treated in our hospital from January 2014 to January 2017 were selected as the objects of laparoscopic radical colon cancer radical surgery. Case inclusion criteria: (1) The diagnostic criteria are in accordance with the relevant regulations of the guidelines for the diagnosis and treatment of colorectal cancer (2015 Edition); (2) Colon cancer was diagnosed by colonoscopy and pathological examination; (3) The TNM stage of colon cancer belongs to I-II stage; (4) Colon cancer with early single lesion; (5) The patient was informed and signed the informed consent. Case exclusion criteria: (1) Colon cancer patients with non-single focus; (2) Patients who were not treated for the first time; (3) Patients combined with other diseases such as endocrine system, coagulation dysfunction, chronic infection, immune system disease and other diseases; (4) Combined with other malignant tumor patients; (5) Highly sensitive patients; (6) Patients with heart, liver and renal insufficiency; (7) Patients with psychiatric disorders.

The cases were divided into the control group and the experimental group according to the random number table method, each with 60 cases. In the control group, there were 36 males and 24 females. The age was 40-67 years old and the mean age (52±8) years old. The control group was (85.10±9.44) mg/mL and (104.95±9.3) U/mL; the experimental group was (71.54±7.31) mg/mL and (91.36±7.08) U/mL. The rate (%) indicated the clinical general enumeration data by using \( \chi^2 \) test. and \( P<0.05 \) a statistically significant difference.

2.2. Experimental method

All cases were treated by laparoscopic radical resection of colon cancer. Water and food were forbidden. Respiratory, pulse, blood pressure and oxygen saturation were monitored closely, and venous access was established. The two groups of anesthetic induction programs were the same, that is: Propofol Injection (purchased from Jiangsu Nhwa Pharmaceutical Co., Ltd., specifications 2 mg/branch from Jiangsu Nhwa Pharmaceutical Co., Ltd., specifications 10 mg/branch, Zununi H20143315), 2-8 \( \mu \)g/(kg h); Propofol Injection, 4-8 mg/(kg h); continuous intravenous infusion. The anesthesia maintenance program in the control group was as follows: Dezocine Injection (purchased from the Yangtze River Pharmaceutical Group Co. Ltd., specifications 5 mg/branch, Zununi H20080329), 20-80 \( \mu \)g/(kg h); Propofol Injection, 4-8 mg/(kg h); continuous intravenous infusion. During operation, 0.05 mg/kg of vecuronium was given discontinuously, in order to maintain muscle relaxation. Thirty min before the end of surgery, infusion of propofol was stopped, remifentanil and dezocine has been given till the end of surgery. After surgery patients who breathed spontaneously were given tracheal extubation and sent into the recovery room.

2.3. Detection index

Ten mL of venous blood were drawn from patients before and after the operation, 5 mL of which was centrifugated for separation of serum. The obtained serum was used to detect and compare the levels of serum GSH, CAT, MDA, SOD, TNF-α, CRP and IL-6 before and after operation in the two groups. The other 5 mL blood was used to detect and compare the levels of CD3\(^+\), CD4\(^+\), CD8\(^+\) and CD4\(^+\)/CD8\(^+\) in the peripheral blood of two groups of children before and after operation.

The levels of serum GSH, CAT, MDA, SOD, TNF-α, CRP and IL-6 were detected by double antibody sandwich enzyme linked immunosorbent assay (ELISA) kit. The levels of peripheral blood CD3\(^+\), CD4\(^+\), CD8\(^+\) and CD4\(^+\)/CD8\(^+\) were detected by Backman CytoFLEX flow cytometry.

2.4. Data analysis

SPSS 19.0 software package was used to process the test result data. Mean ± standard deviation Mean ± SD represented measurement data. \( t \) test was adopted to compare the difference between groups. The rate (%) indicated the clinical general enumeration data by using \( \chi^2 \) test. and \( P<0.05 \) a statistically significant difference.

3. Results

3.1. Comparison of serum GSH, CAT levels before and after operation in the two groups

Before operation, the levels of serum GSH and CAT in the control group were (85.10±9.44) mg/mL and (104.95±9.3) U/mL respectively while serum levels in experimental group were (84.93±10.02) mg/mL and (105.13±8.71) U/mL, there was no significant difference between the two groups (\( P>0.05 \)); After operation, the levels of serum GSH and CAT in the control group were (59.43±6.89) mg/mL and (80.30±6.26) U/mL respectively while those levels in experimental group were (71.54±7.31) mg/mL and (91.36±7.08) U/mL. The serum GSH and CAT levels of the
two groups were lower than those before operation, and the levels of serum GSH and CAT in the experimental group were all better than those in the control group, with significant difference (P<0.05)(Table 1).

**Table 1.**
Comparison of serum GSH, CAT levels before and after operation in the two groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>GSH (mg/mL)</th>
<th>CAT (U/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>60</td>
<td>Before operation</td>
<td>85.10±9.44</td>
<td>104.95±9.32</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After operation</td>
<td>59.43±6.89</td>
<td>80.30±6.26</td>
</tr>
<tr>
<td>Experimental group</td>
<td>60</td>
<td>Before operation</td>
<td>84.93±10.02</td>
<td>105.13±8.71</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After operation</td>
<td>71.54±7.31</td>
<td>91.36±7.08</td>
</tr>
</tbody>
</table>

Compared with pre operation, P<0.05; compared with the control group, *P<0.05.

### 3.2. Comparison of serum MDA, SOD levels before and after operation in the two groups

Before operation, the levels of serum MDA, SOD in the control group were respectively (3.14±0.25) mmol/L and (97.31±9.11) nU/mL, while the levels in experimental group were (3.20±0.32) mmol/L and (97.03±9.52) nU/mL. There was no significant difference between the two groups (P>0.05); After operation, the levels of serum MDA, SOD in the control group were respectively (8.05±0.84) mmol/L and (71.24±6.50) nU/mL while the levels in experimental group were (5.74±0.61) mmol/L and (82.45±7.48) nU/mL. The serum SOD level of the two groups after operation was lower than that before operation, and the serum MDA level was higher than that before operation. The serum MDA and SOD levels in the experimental group were all better than those in the control group, with significant difference (P<0.05)(Table 2).

**Table 2.**
Comparison of serum MDA, SOD levels before and after operation in the two groups (ug/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>MDA (mmol/L)</th>
<th>SOD (nU/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>60</td>
<td>Before operation</td>
<td>3.14±0.25</td>
<td>97.31±9.11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After operation</td>
<td>8.05±0.84</td>
<td>71.24±6.50</td>
</tr>
<tr>
<td>Experimental group</td>
<td>60</td>
<td>Before operation</td>
<td>3.20±0.32</td>
<td>97.03±9.52</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After operation</td>
<td>5.74±0.61</td>
<td>82.45±7.48</td>
</tr>
</tbody>
</table>

Compared with pre operation, P<0.05; compared with the control group, *P<0.05.

### 3.3. Comparison of serum TNF-α , CRP, IL-6 levels before and after operation in the two groups

Before operation, the levels of serum TNF-α, CRP, IL-6 in the control group were respectively (26.30±2.87) pg/mL, (5.10±0.43) mg/L, (16.51±2.12) pg/mL, that in experimental group were (26.72±3.01) pg/mL, (5.23±0.51) mg/L, (16.87±2.25) pg/mL, there was no significant difference between the two groups (P>0.05); After operation, the levels of serum TNF-α, CRP, IL-6 in the control group were respectively (52.41±4.89) pg/mL, (20.84±2.86) mg/L, (73.25±6.72) pg/mL, that in experimental group were (38.20±3.75) pg/mL, (11.38±1.47) mg/L, (49.60±4.11) pg/mL, the serum levels of TNF-α, CRP and IL-6 in the two groups were higher than those before operation, and the levels of serum TNF-α, CRP and IL-6 in the experimental group were lower than those in the control group after operation (P<0.05)(Table 3).

### 3.4. Comparison of the level of T lymphocyte subsets in peripheral blood of two groups before and after treatment

Before operation, the levels of CD3+, CD4+, CD8+ and CD4+/CD8+ in the peripheral blood of the control group were (54.96±6.05)%, (34.95±3.84)%, (21.14±2.03)%, and (1.65±0.17), respectively while these levels in experimental group were (54.71±6.13)%, (34.76±3.90)%, (21.62±2.35)%, and (1.61±0.20). There was no significant difference between the two groups (P>0.05); After operation, the levels of CD3+, CD4+, CD8+ and CD4+/CD8+ in the peripheral blood of the control group were (39.52±3.66)%, (20.24±2.02)%, (25.69±3.11)%, and (0.79±0.08) respectively while these levels in experimental group were (48.30±4.27)%, (27.12±2.75)%, (23.82±2.63)%, and (1.14±0.12). The levels of CD3+ and CD4+ in peripheral blood and CD4+/CD8+ in two groups were lower than those before operation, and CD8+ level was higher than that before operation. The levels of CD3+, CD4+, CD8+ and CD4+/CD8+ in the experimental group were better than those in the control group after operation (P<0.05)(Table 4).

**Table 3.**
Comparison of serum TNF-α, CRP, IL-6 levels before and after operation in the two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>TNF-α (pg/mL)</th>
<th>CRP (mg/L)</th>
<th>IL-6 (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>60</td>
<td>Before operation</td>
<td>26.30±2.87</td>
<td>5.10±0.43</td>
<td>16.51±2.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After operation</td>
<td>52.41±4.89</td>
<td>20.84±2.86</td>
<td>73.25±6.72</td>
</tr>
<tr>
<td>Experimental group</td>
<td>60</td>
<td>Before operation</td>
<td>26.72±3.01</td>
<td>5.23±0.51</td>
<td>16.87±2.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After operation</td>
<td>38.20±3.75</td>
<td>11.38±1.47</td>
<td>49.60±4.11</td>
</tr>
</tbody>
</table>

Note: compared with pre operation, P<0.05; compared with the control group, *P<0.05.

**Table 4.**
Comparison of the level of T lymphocyte subsets in peripheral blood of two groups before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>CD3+(%)</th>
<th>CD4+(%)</th>
<th>CD8+(%)</th>
<th>CD4+/CD8+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>60</td>
<td>Before operation</td>
<td>54.96±6.05</td>
<td>34.95±3.84</td>
<td>21.14±2.03</td>
<td>1.65±0.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After operation</td>
<td>39.52±3.66</td>
<td>20.24±2.02</td>
<td>25.69±3.11</td>
<td>0.79±0.08</td>
</tr>
<tr>
<td>Experimental group</td>
<td>60</td>
<td>Before operation</td>
<td>54.71±6.13</td>
<td>34.76±3.90</td>
<td>21.62±2.35</td>
<td>1.61±0.20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After operation</td>
<td>48.30±4.27</td>
<td>27.12±2.75</td>
<td>23.82±2.63</td>
<td>1.14±0.12</td>
</tr>
</tbody>
</table>

Compared with pre operation, P<0.05; compared with the control group, *P<0.05.
4. Discussion

The pathogenesis of colon cancer is still unclear so far. It is considered to be mainly related to the factors such as heredity, high fat diet, deficiency of cellulose and so on[8,9]. Laparoscopic technique has the advantages of small trauma and rapid recovery. However, there is still stress injury in the perioperative period[10]. Perioperative stress reaction can lead to immune dysfunction, abnormal release of cytokines and cortisol, and other inflammatory complications[11]. At present, remifentanil combined with anesthesia was used clinically to reduce the stress response of the operation patients, however, there is a risk of postoperative agitation and pain allergy[12]. Dezocine is an opioid analgesic. On the one hand, it inhibits nerve impulse transmission by reducing the production of adenylate cyclase, thereby exerting analgesic effect. On the other hand, it can reduce the inhibition of u receptors and reduce the inhibition of macrophages and T lymphocytes to reduce cellular immune function[13-15]. This study was to explore the effects of dezocine combined with anesthesia on serum GSH, CAT, MDA, SOD, TNF-α, CRP, IL-6 and T lymphocyte subsets in patients after laparoscopic surgery for colon cancer, in order to provide some inspiration for alleviating the stress damage in patients with laparoscopic colon cancer surgery.

The results of this study show that the serum GSH, CAT and SOD levels of the two groups were lower than those before operation, and the level of serum MDA was higher than that before operation. The levels of serum GSH, CAT, MDA and SOD in the experimental group were all better than those in the control group, with significant difference (P<0.05). This suggests that the methods of dezocine combined with anesthesia for patients after laparoscopic surgery for colon cancer can reduce the oxidative stress reaction after operation. Pneumoperitoneum needs to be established during the implementation of laparoscopy, which causes intraoperative ischemia of the abdominal organs, combined with postoperative blood flow recovery. Ischemia reperfusion can cause antioxidant activities such as GSH, CAT and SOD to decrease, and MDA and other oxidation products increase, resulting in oxidative stress injury[16,17]. It has been reported that the application of dezocine in operation could inhibit the excessive release of inflammatory mediators and inflammatory factors, so as to reduce tissue damage[18]. In addition, the results of this study show that the levels of CD3+ and CD4+ in peripheral blood and CD4+/CD8+ in two groups were lower than those before operation, and CD8+ level was higher than that before operation. The levels of CD3+, CD4+, CD8+ and CD4+/CD8+ in the experimental group were better than those in the control group after operation, with significant difference (P<0.05). This suggests that dezocine combined with anesthesia has small effect on cellular immune function in patients after laparoscopic surgery for colon cancer. Oxidative stress in the perioperative period can lead to the disorder of immune function in patients while dezocine can alleviate inhibition of macrophages and T lymphocytes by antagonizing u receptor, which helps to prevent cellular immunity[19].

In summary, dezocine combined with anesthesia can reduce the oxidative stress reaction in patients after laparoscopic surgery for colon cancer, lower serum TNF-a, CRP, IL-6 levels, and has smaller effect on cellular immune function. Thus it is worthy of clinical application.

References

[22] Han, Xu Wenti, Wu Hefen. Study on the effect of laparoscopic surgery on colorectal cancer patients with IL-6, MDA and SOD levels of dezocine anesthesia. Chin Pharm J 2016; 36(4): 102-104.