Effect of dexmedetomidine on inflammatory factors and immune function in elderly patients undergoing laparoscopic radical resection of colorectal cancer

Jian-Xin Zhang 1,*, Yan-Jun Li 2, Bing-Bing Liu 1, Xiao-Jing Peng 1, Ping-Xuan Guo 1

1. Anesthesia Department, Kailuan General Hospital of Hebei Province, Tangshan City 063000
2. Gastrointestinal Endoscopy Room, Qianxi people’s Hospital of Hebei Province, Tangshan City 064300

ARTICLE INFO

Article history:
Received 12 Jun 2017
Received in revised form 19 Jun 2017
Accepted 3 Jul 2017
Available online 14 Jul 2017

Keywords:
Dexmedetomidine
Elderly
Laparoscopy
Radical resection of colorectal cancer
Inflammatory factors
Immune function

ABSTRACT

Objective: To investigate the effect of dexmedetomidine on inflammatory factors and immune function in elderly patients undergoing laparoscopic radical resection of colorectal cancer.

Methods: From April 2016 to April 2017, 86 cases of elderly laparoscopic radical resection of colorectal cancer in our hospital were selected and randomly divided into the observation group and the control group. 2 groups of patients were open venous access, oxygen mask, monitoring heart rate (HR), blood pressure (BP), electrocardiogram (ECG), oxygen saturation (SpO2), bispectral index (BIS), after induction of anesthesia, the observation group was given dexmedetomidine 0.4 g/kg to 20 mL of normal saline control. Group of 20 mL saline, 15 min infusion is completed, and the observation group of dexmedetomidine in 0.4 g/kg - h continuous infusion of normal saline control group, continuous infusion, until the end of surgery. Before induction of anesthesia (T0), 2 h after operation beginning (T1), at the end of operation (T2), 24 h after operation (T3) in venous blood, using ELISA method for the determination of serum interleukin-2 receptor (sIL-2R) and interleukin-6 (IL-6), tumor necrosis factor alpha (the level of TNF-alpha); on preoperative and postoperative 4 h, 12 h, 24 h after operation in venous blood serum epinephrine ELISA method (E), norepinephrine (NE), endothelin-1 (ET-1) level; on preoperative and postoperative 4 h, 12 h, 24 h after surgery, 24 h venous blood flow cytometry determination of CD3+, CD4+, CD8+, CD4+/CD8+. Results: compared with before operation, the observation group after 4 h, 12 h, 24 h NE, ET-1 increased, the observation group after 4 h, 12 h, 24 h E increased, the control group after 4 h, 12 h, 24 h NE was lower than that of the control group; compared with the preoperative, 2 group after 4 h, 12 h, 24 h CD3+, CD4+, CD8+ and CD4+/CD8+ decreased, the observation group after 4 h, 12 h, 24 h CD3+, CD4+ higher than those in the control group. Conclusion: Dexmedetomidine has a good analgesic effect on elderly patients undergoing laparoscopic radical resection of colorectal cancer. It can effectively relieve the stress reaction and inflammatory reaction during perioperative period, and effectively improve the immune function of the patients.

1. Introduction

Colorectal cancer is the most common malignant tumor in the digestive system, and radical resection is the best treatment.

Laparoscopic surgery with less trauma, quicker recovery, shorter hospitalization time and other advantages, the elderly patients in the treatment tend to laparoscopic minimally invasive surgery, but due to the decline of the body organ compensatory function, strong stress response caused by CO2 pneumoperitoneum, resulting in changes of neuroendocrine system and immune system, caused by hormones and cytokines change[1]. Studies have shown that dexmedetomidine can alleviate the inflammatory response and stabilize hemodynamics by blocking the activity of the sympathetic nerve center and alleviating the stress response[2]. In this study, 86 cases of laparoscopic radical resection of colorectal cancer in our
hospital from April 2016 to April 2017 were studied to investigate the influence of dexmedetomidine on perioperative inflammatory factors and immune function.

2. Clinical information

2.1. General information

From April 2016 to April 2017 in our hospital for the elderly laparoscopic resection of colorectal cancer patients with 86 cases as the research object, the American Society of anesthesiologists (ASA) grade I-II, heart, liver, lung and kidney function, patients and their families and signed the informed consent, and the exclusion of significant bradycardia, atrioventricular block, ventricular arrhythmia, endocrine system diseases, blood diseases, mental disorders and related to drug allergy. The rats were randomly divided into observation group and control group. There were 43 cases in the observation group, 27 males and 16 females. The average age was (68±4) years old, and the weight was 47-72 kg, and the mean (61.5±5.7) kg was 61-77. The control group consisted of 43 cases, 28 males and 15 females, aged 62-77 years, mean (68±4) years old, weight 48-73 kg, mean (62.4±5.8) kg. There was no significant difference between the 2 groups in terms of age, sex, weight (P>0.05).

2.2. Method

2 groups of patients were open venous access, mask oxygen inhalation, monitoring heart rate (HR), blood pressure (BP), electrocardiogram (ECG), blood oxygen saturation (SpO2), bispectral index (BIS) value. Anesthesia was induced by intravenous injection of fentanyl 4-6 g/kg, cisatracurium 0.15 mg/kg, midazolam 0.04 mg/kg, propofol TCI (target plasma concentration of 4 g/mL), after fentanyl 4-6 g/kg, cisatracurium 0.15 mg/kg, midazolam 0.04 mg/kg, propofol TCI (target plasma concentration of 4 g/mL), after fentanyl 4-6 g/kg, cisatracurium 0.15 mg/kg, midazolam 0.04 mg/kg.

2.3 Observation index

(1) inflammatory factors: before induction of anesthesia (T0), 2 h after operation beginning (T1), at the end of operation (T2), 24 h after operation (T3), venous blood was collected before operation, 4 h, 12 h after operation, serum levels of epinephrine (E), norepinephrine (NE) and endothelin-1 (ET-1) were measured by ELISA. (3) immune function: venous blood was collected before operation, 4 h, 12 h after operation, and 24 h after operation. CD4\(^+\), CD8\(^+\), CD4/CD8 ratio were measured by flow cytometry.

3. Result

3.1. Changes of inflammatory factors at different times

Compared with T0, the T1, T2, sIL-2R, IL-6 and TNF-alpha in both groups were increased (P<0.05), while those of the observation group, T1 and T2, sIL-2R, IL-6 and TNF-alpha, were lower than those in the control group (P<0.05) at the same time. See Table 1.

Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>sIL-2R (pg/mL)</th>
<th>IL-6 (pg/mL)</th>
<th>TNF-α (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>T0</td>
<td>62.54±5.71</td>
<td>14.54±4.85</td>
<td>17.63±6.23</td>
</tr>
<tr>
<td>Group</td>
<td>T1</td>
<td>73.56±5.74 (a)</td>
<td>27.52±6.81</td>
<td>35.74±6.13 (a)</td>
</tr>
<tr>
<td>Control group</td>
<td>T0</td>
<td>104.75±12.78</td>
<td>41.54±6.85</td>
<td>57.65±6.81</td>
</tr>
<tr>
<td>Group</td>
<td>T1</td>
<td>107.69±13.84</td>
<td>45.29±5.74</td>
<td>65.77±7.45</td>
</tr>
<tr>
<td>Control group</td>
<td>T2</td>
<td>108.95±14.36</td>
<td>48.72±7.38</td>
<td>68.27±6.92(b)</td>
</tr>
</tbody>
</table>

Note: compared with the same group \(P<0.05\), \(T_0\), compared with the control group \(P<0.05\).

3.2. Changes of stress indexes at different times

Compared with before operation, the observation group after 4 h, 12 h, 24 h NE (P<0.05), and the lower control group E, NE and ET-1 increased (P<0.05), the observation group after 4 h, 12 h, 24 h, NE, ET-1 lower than that of the control group (P<0.05). See table 2.

Table 2.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>E (ng/L)</th>
<th>NE (ng/L)</th>
<th>ET-1 (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Preoperative</td>
<td>59.76±15.45</td>
<td>587.36±98.57</td>
<td>141.26±24.36</td>
</tr>
<tr>
<td>Group</td>
<td>4 h postoperatively</td>
<td>60.54±16.28 (a)</td>
<td>475.41±114.37 (a)</td>
<td>143.56±27.37 (a)</td>
</tr>
<tr>
<td>Control group</td>
<td>Preoperative</td>
<td>58.85±15.23</td>
<td>489.56±102.31</td>
<td>141.38±26.11</td>
</tr>
<tr>
<td>Group</td>
<td>4 h postoperatively</td>
<td>65.71±15.23 (a)</td>
<td>557.45±125.32 (a)</td>
<td>179.63±37.26 (a)</td>
</tr>
<tr>
<td>Control group</td>
<td>12 h postoperatively</td>
<td>67.45±15.36 (a)</td>
<td>518.57±102.63 (a)</td>
<td>174.37±26.75 (a)</td>
</tr>
<tr>
<td>Group</td>
<td>24 h postoperatively</td>
<td>63.15±14.62</td>
<td>505.78±103.29 (a)</td>
<td>165.45±29.34 (a)</td>
</tr>
</tbody>
</table>

Note: compared with the same group before operation, \(P<0.05\), compared with the control group \(P<0.05\).
For the record, the inflammatory response mediated by anesthesia and surgical trauma can cause systemic acute phase reactions and cause changes in the levels of peripheral and central inflammatory factors in patients. Elderly patients with tumor immunity decline, coupled with strong perioperative stress response, release of inflammatory mediators, will destroy the balance of cytokines, interfering with the immune system. Small intestine-2R is a low affinity receptor, mainly derived from activated T lymphocyte membrane receptor protein on the cell membrane, and small intestine-2R combined with IL-2, the proliferation and function of immune cells, inhibit tumor cell division and proliferation, thereby inhibiting the immune response. IL-6 is a multifunctional inflammatory cytokine. It is a key component of inflammatory mediators and closely related to the occurrence and development of tumors. TNF-alpha is a cytokine with dual biological effects, such as anti-infective, anti-tumor effect under normal circumstances, when more than a certain amount, but with the occurrence and development of other inflammatory factors to promote cancer, and produce a variety of pathological damage. The study confirmed that, dexmedetomidine has anti-inflammatory effect and its mechanism of dexmedetomidine can inhibit sympathetic activity and activation of cholinergic anti-inflammatory pathway, activation of imidazoline receptor play an anti-inflammatory effect and regulation of nuclear factor kappa B to inflammatory pathway, activation of imidazoline receptor play an anti-inflammatory effect and regulation of nuclear factor kappa B to inflammatory pathway. In patients with colorectal cancer and anti-inflammatory effects of promoting the system of thought of dexmedetomidine and ulinastatin has anti-inflammatory effect, can effectively reduce the expression of IL-6, TNF-alpha and other inflammatory factors, antagonistic cytotoxic proteases and oxygen free radicals. To reduce the damage of tissue and organ inflammation. This study shows that, compared with T0, 2 patients in group T2, T3 small intestine-2R, IL-6, TNF-alpha were increased (P<0.05), the observation group T2, T3 small intestine-2R, IL-6, TNF-alpha were lower than that of the control group (P<0.05), suggesting that dexmedetomidine can reduce elderly laparoscopic colorectal cancer radical stress reaction of surgery during the surgery, reduce inflammation.

### Table 3

Changes of immune indexes at different time.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>T0 (%)</th>
<th>T4 (%)</th>
<th>T12 (%)</th>
<th>T24 (%)</th>
<th>T6 (%)</th>
<th>T12 (%)</th>
<th>T24 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Preoperative</td>
<td>61.36±5.48</td>
<td>37.23±4.51</td>
<td>32.13±3.41</td>
<td>1.48±0.71</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 h</td>
<td>53.82±3.55</td>
<td>29.64±5.17</td>
<td>28.54±3.17</td>
<td>1.19±0.43</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 h</td>
<td>48.74±4.75</td>
<td>26.74±3.78</td>
<td>26.45±4.07</td>
<td>1.02±0.35</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 h</td>
<td>55.71±4.12</td>
<td>33.41±4.26</td>
<td>29.25±5.36</td>
<td>1.32±0.57</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Preoperative</td>
<td>60.57±5.63</td>
<td>37.31±5.19</td>
<td>33.07±4.02</td>
<td>1.49±0.69</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 h</td>
<td>46.56±6.23</td>
<td>26.12±5.38</td>
<td>25.15±4.13</td>
<td>1.05±0.52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 h</td>
<td>44.37±5.65</td>
<td>24.23±4.38</td>
<td>22.08±3.16</td>
<td>0.91±0.27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 h</td>
<td>52.70±7.23</td>
<td>30.68±5.09</td>
<td>27.27±4.11</td>
<td>1.21±0.37</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: compared with the same group before operation, *P<0.05, compared with the control group, **P<0.05.

### 3.3 Changes of immune index at different time

Compared with the preoperative, 2 group after 4 h, 12 h, 24 h CD4+, CD8+ and CD4+/CD8+ decreased (P<0.05), the observation group after 4 h, 12 h, 24 h CD4+, CD8+, CD4+/CD8+ higher than those in the control group (P<0.05). See table 3.

### 4. Discussion

Laparoscopic diagnosis and treatment of diseases is a reliable and safe method, but it can cause stress, significantly increased release of catecholamine (CA), the sympathetic nervous excitation, resulting in HR, BP wave, especially in the elderly population, the decline in physical function, the compensatory function, the relative lack of response on the stress coping ability, not only affects the operation after recovery[3], will increase the complications. Dexmedetomidine is a highly selective alpha 2 adrenergic receptor agonist, can inhibit sympathetic NE release, play a central role in anti-sympathetic, but also has the effect of anti-anxiety, analgesic, make the patient into the natural non REM sleep, and less influence on cognitive function in patients with[4]. Studies have shown that[5], surgery and postoperative pain and other stimuli can cause stress response, increase the release of CA, lead to intracellular calcium overload, thereby promoting inflammation and high reactivity, affecting the prognosis of patients[6]. It has been reported to reduce the inflammatory response by reducing perioperative E, NE, cortisol (COR), and blood glucose levels in patients with dexmedetomidine. Another scholar reported that[7], continuous intravenous infusion of dexmedetomidine can effectively reduce the injury of the operation to stimulate the body, reduce the nerve endocrine response, and effectively inhibit the stress response. This study shows that, compared with that before operation, the observation group after 4 h, 12 h, 24 h NE (P<0.05), and the lower control group E, NE and ET-1 increased (P<0.05), the observation group after 4 h, 12 h, 24 h E, NE, ET-1 lower than the control group (P<0.05), suggesting that dexmedetomidine can reduce the elderly patients undergoing gastrectomy with stress of laparoscopic colorectal cancer.

To reduce the damage of tissue and organ inflammation[13]. This study shows that, compared with T0, 2 patients in group T2, T3 small intestine-2R, IL-6, TNF-alpha were increased (P<0.05), the observation group T2, T3 small intestine-2R, IL-6, TNF-alpha were lower than that of the control group (P<0.05), suggesting that dexmedetomidine can reduce elderly laparoscopic colorectal cancer radical stress reaction of surgery during the surgery, reduce inflammation.
Reduce the elderly patients with cancer of the body T cell proliferation, decreased immune response mediated by the patients, the relatively low immune function, and tumor cells can activate immune inhibitory factor, further inhibit the immune function[14]. Studies have shown that[15], trauma, anesthesia, drug use and stress reaction can influence the perioperative immune status of the patients. It has been reported that dexmedetomidine can modulate the immune response in elderly patients undergoing laparoscopic surgery, reduce the release of inflammatory mediators, relieve stress response, and improve the immune function of patients[16]. This study shows that, compared with the preoperative, 2 group after 4 h, 12 h, 24 h CD3+, CD4+, CD8+ and CD4+/CD8+ decreased (P<0.05), the observation group after 4 h, 12 h, 24 h CD3+, CD4+, CD8+, CD4+/ CD8+ higher than those in the control group (P<0.05), suggesting that dexmedetomidine can improve old laparoscopic colorectal cancer radical surgery in patients with perioperative immune function.

To sum up, dexmedetomidine has a good analgesic effect in elderly patients undergoing laparoscopic radical resection of colorectal cancer. It can effectively relieve the stress reaction and inflammatory reaction during perioperative period, and effectively improve the immune function of the patients.

Reference