Effect of dexmedetomidine on the immune function, serum inflammatory factors and hemodynamics in elderly patients with gastric cancer

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ABSTRACT

Objective: To investigate the effect of dexmedetomidine on the immune function, serum inflammatory factors and hemodynamics in elderly patients with gastric cancer. Method: A total of 84 elderly patients with gastric cancer treated in our hospital from September 2015 to March 2017 were randomly divided into the control group and the observation group, each with 42 cases. The control group received intravenous infusion of Sodium Chloride Injection before anesthesia induction, and the observation group received dexmedetomidine intravenous infusion. The levels of hemodynamic indexes HR and MAP levels, serum inflammatory factors levels of CRP, IL-2, IL-10 levels and T lymphocyte subsets levels were compared between the two groups. Results: Compared with induction of anesthesia before, the HR level of two groups were both significantly increased at 6 h after operation, the MAP level of control group was significantly increased at 6 h after operation while was not changed significantly in the observation group. According comparison between groups at 6 h after operation, the levels of HR, MAP in observation group were significantly lower than those of the control group. Compared with induction of anesthesia before, the CRP level was significantly increased at each postoperative time point in two groups; the IL-2 level at 24 h after operation of two groups were decreased significantly, while both increased back and significantly higher than that before induction of anesthesia; the IL-10 level at 24 h after operation of two groups were increased significantly, while both decreased back and significantly lower than that before induction of anesthesia. Compared with the control group at the same time point, the CRP, IL-10 level of observation group were significantly lower than those of the control group and the IL-2 level of observation group was significantly higher than that of the control group. Compared with induction of anesthesia before, the levels of CD3, CD4, CD4/CD8 of control group were significantly decreased at 6 h, 24 h, 72 h after operation and significantly decreased at 24 h after operation in observation group. 72 h after operation, the levels of CD3, CD4, CD4/CD8 of observation group increased back and were not changed significantly compared with induction of anesthesia before. Conclusion: Dexmedetomidine for elderly patients with gastric cancer assisted anesthesia can reduce the stress caused by surgical trauma, improve the immune level, reduce the inflammatory response, and stabilize hemodynamics of patients in the perioperative period significantly. It is worthy of clinical promotion.

1. Introduction

Gastric cancer is a common malignant tumor of digestive system, with high morbidity and mortality. The main surgical treatment is surgical resection. Surgery and anesthesia stimulate the body’s stress response, resulting in immune suppression, and trigger inflammatory response and hemodynamic changes, increase the proliferation of cancer cells and the risk of postoperative recurrence[1-2]. Different anesthesia methods and drugs have great influence on the body. Among them, dexmedetomidine can inhibit sympathetic activity and sedative and analgesic effect, and auxiliary anesthesia can alleviate the stress reaction caused by surgical trauma moderately, so it has great potential for clinical application[3,4]. This study aimed to
investigate the effects of dexmedetomidine on perioperative immune function, inflammatory factors and hemodynamics in elderly patients with gastric cancer.

2. Data and methods

2.1 General information

In this study, 84 cases of elderly patients with gastric cancer who were treated in our hospital from September 2015 to March 2017 were selected. Classification of anesthesia grade I to II. According to the random number table method, they were divided into control group and observation group with 42 cases in each group. The control group consisted of 24 males and 18 females, aged 63 to 77 years old, with 29 cases of TNM stage I to II, and 13 cases of stage III to IV. The observation group consisted of 26 males and 16 females, aged 65 to 76 years old. The TNM stage was from stage I to stage II in 28 cases, and stage III to IV in 14 cases. All patients met the diagnostic criteria of gastric cancer[5]. The medical ethics committee approved the informed consent of the patients and their families and signed the informed consent form. Case exclusion criteria: Preoperative radiotherapy and chemotherapy and blood transfusion treatment were carried out; Autoimmune diseases with metabolic or endocrine diseases; Preoperative infection occurred; Perioperative blood transfusion occurred; Combined with severe cardiovascular disease; Have a history of mental illness; Those with immune system diseases or endocrine diseases. There was no significant difference in general data between the two groups ($P>0.05$).

2.2 Anesthesia methods

All patients were on blood pressure, pulse, ECG monitoring after the burglary, open the right internal jugular vein passage, and intravenous injection of 6-8 mL/(kg•h) sodium lactate Ringer’s solution. Preoperative 30 min, the observation group received intravenous infusion of 0.5 g/kg dexmedetomidine for 10 min (Jiangsu nhwa pharmaceutical Limited by Share Ltd, National medical term H20110085). Intravenous infusion was performed at 0.3 g/(kg.h) until the end of operation. The control group received medical term H20110085). Intravenous infusion of 0.5 g/kg dexmedetomidine for 10 min by General Company GELOGIQ-3 color Doppler ultrasonic diagnostic apparatus.

2.4 Statistical processing

Result data was analyzed and processed by SPSS 17.0 statistical software. T lymphocyte subsets CD3+, CD4+, CD4+/CD8+ levels, serum inflammatory factors CRP, IL-2, IL-10 levels and hemodynamic indexes HR and MAP levels were normal distribution, expressed as Mean ± SD. The t test was used to compare the groups before and after anesthesia induction in each time point. $P<0.05$ showed significant difference, with statistical significance.

3. Result

3.1 Comparison of hemodynamics between two groups before and after treatment

Compared with before anesthesia induction, the 6 h levels of HR in two groups were significantly increased ($P<0.05$), and the level of MAP in the control group was significantly higher after 6 h ($P<0.05$), while the level of MAP in the observation group was not significantly changed ($P>0.05$). Compared with the control group, the 6 h level of HR in the observation group was (70.11±5.81) times/min and MAP level was (87.28±10.34) mmHg, which was significantly lower than that of the control group ($P<0.05$). See Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>HR (times/min)</th>
<th>MAP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before anesthesia induction</td>
<td>66.84±5.93</td>
<td>86.14±10.35</td>
</tr>
<tr>
<td></td>
<td>Postoperative 6 h</td>
<td>81.02±5.81</td>
<td>94.28±11.08</td>
</tr>
<tr>
<td></td>
<td>Before anesthesia induction</td>
<td>66.71±5.85</td>
<td>86.32±10.09</td>
</tr>
<tr>
<td></td>
<td>Postoperative 6 h</td>
<td>70.11±5.80</td>
<td>87.28±10.34</td>
</tr>
</tbody>
</table>

Note: compared with before anesthesia induction, $P<0.05$; compared with the control group at the same time, $P<0.05$.
3.2 Comparison of serum inflammatory factor levels between two groups before and after treatment

Compared with before anesthesia induction: The levels of CRP were significantly increased at each time point (P<0.05) in the two groups, the level of 24 h in the two groups decreased significantly after operation (P<0.05), but decreased at 72 h after operation, and significantly increased compared with that before anesthesia (P<0.05). The IL-10 in two groups increased significantly at 24 h after operation (P<0.05), but decreased at 72 h after operation and decreased significantly compared with that before induction (P<0.05). Compared with the control group, the levels of CRP and IL-10 in the observation group after 6 h, 24 h, 72 h were significantly lower than those in the control group, the level of IL-2 was significantly higher than that of the control group, the differences were statistically significant (P<0.05). See table 2.

3.3 Comparison of lymphocyte subsets before and after treatment in two groups

Compared with before anesthesia induction, the levels of CD3+, CD4+ and CD4+/CD8+ in the control group after 6 h, 24 h and 72 h were significantly decreased (P<0.05). In the observation group, the above indexes decreased significantly after 24 h (P<0.05), but recovered at 72 h after operation, and had no obvious change compared with that before anesthesia induction (P>0.05). At the same time, the levels of CD3+, CD4+ and CD4+/CD8+ in the observation group at 6 h, 24 h and 72 h after operation were significantly higher than those in the control group (P<0.05). See table 3.

### Table 2.
Comparison of serum inflammatory factors between the two groups before and after treatment (n=42).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>CRP (mg/L)</th>
<th>IL-2 (ng/L)</th>
<th>IL-10 (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>Before anesthesia induction</td>
<td>9.67±3.15</td>
<td>81.07±8.67</td>
<td>158.42±14.57</td>
</tr>
<tr>
<td></td>
<td>Postoperative 6 h</td>
<td>20.84±3.77</td>
<td>52.84±8.04</td>
<td>178.14±14.17</td>
</tr>
<tr>
<td></td>
<td>Postoperative 24 h</td>
<td>27.13±4.04</td>
<td>51.39±7.95</td>
<td>185.49±14.27</td>
</tr>
<tr>
<td></td>
<td>Postoperative 72 h</td>
<td>32.57±4.85</td>
<td>90.11±8.91</td>
<td>130.47±12.51</td>
</tr>
<tr>
<td>Observation group</td>
<td>Before anesthesia induction</td>
<td>9.57±4.01</td>
<td>80.85±7.61</td>
<td>160.13±15.04</td>
</tr>
<tr>
<td></td>
<td>Postoperative 6 h</td>
<td>16.09±3.75</td>
<td>71.42±7.63</td>
<td>171.33±13.42</td>
</tr>
<tr>
<td></td>
<td>Postoperative 24 h</td>
<td>18.82±3.81</td>
<td>69.31±7.04</td>
<td>175.84±14.92</td>
</tr>
<tr>
<td></td>
<td>Postoperative 72 h</td>
<td>21.63±4.18</td>
<td>102.57±9.32</td>
<td>103.97±13.55</td>
</tr>
</tbody>
</table>

Note: compared with before anesthesia induction, P<0.05, compared with the control group at the same time, P<0.05.

### Table 3.
Comparison of lymphocyte subsets between the two groups before and after treatment (n=42).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>CD3+ (%)</th>
<th>CD4+ (%)</th>
<th>CD4+/CD8+ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>Before anesthesia induction</td>
<td>58.02±5.44</td>
<td>37.84±4.58</td>
<td>1.78±0.37</td>
</tr>
<tr>
<td></td>
<td>Postoperative 6 h</td>
<td>47.18±5.32</td>
<td>29.91±5.03</td>
<td>1.21±0.43</td>
</tr>
<tr>
<td></td>
<td>Postoperative 24 h</td>
<td>36.92±4.91</td>
<td>24.05±4.91</td>
<td>1.12±0.39</td>
</tr>
<tr>
<td></td>
<td>Postoperative 72 h</td>
<td>42.84±5.04</td>
<td>26.32±5.73</td>
<td>1.41±0.45</td>
</tr>
<tr>
<td>Observation group</td>
<td>Before anesthesia induction</td>
<td>57.83±5.21</td>
<td>37.61±5.69</td>
<td>1.76±0.32</td>
</tr>
<tr>
<td></td>
<td>Postoperative 6 h</td>
<td>56.21±4.74</td>
<td>36.01±5.24</td>
<td>1.47±0.31</td>
</tr>
<tr>
<td></td>
<td>Postoperative 24 h</td>
<td>52.32±5.81</td>
<td>32.20±5.44</td>
<td>1.42±0.30</td>
</tr>
<tr>
<td></td>
<td>Postoperative 72 h</td>
<td>56.53±5.88</td>
<td>36.03±6.01</td>
<td>1.64±0.38</td>
</tr>
</tbody>
</table>

Note: compared with before anesthesia induction, P<0.05; compared with the control group at the same time, P<0.05.

4. Discussion

Gastric cancer is the first malignant tumor in China, and the incidence is increasing in recent years. At present, the main surgical treatment is surgical resection, but because of surgical trauma, long time, it will cause the patient to produce a strong stress reaction, and increase catecholamine. Catecholamine can stimulate the adrenergic α and β receptors, resulting in a series of hemodynamic changes in patients with higher heart rate and higher blood pressure[6-9]. Surgical trauma, anesthesia and postoperative pain will aggravate the damage of immune function, and increase the content of inflammatory factors, thus damage the organs and increase the risk of tumor recurrence and metastasis. Surgical trauma, anesthesia and postoperative pain will aggravate the damage of immune function, and increase the content of inflammatory factors, thus damage the organs and increase the risk of tumor recurrence and metastasis[10]. Research shows[11], the stress response of patients to surgical trauma can lead to neuroendocrine changes in the nervous system, which may be the main cause of immunosuppression. Therefore, the rational selection of anesthetic methods and anesthetics in the process of anesthesia plays a positive role in suppressing the stress reaction during the operation.

Dexmedetomidine is an intravenous sedative drug widely used in clinic, and it is a highly selective α-2 adrenoceptor agonist. It commonly used in anesthesia, can play a sedative, anti-inflammatory, analgesic anti-sympathetic function, can activate the cholinergic anti-
inflammatory pathway, reduce the levels of inflammatory factors, and not on the breathing of patients have obvious inhibition. At the same time, dexmedetomidine can maintain cardiovascular stability during induction of anesthesia maintenance\(^{[12,13]}\). Hemodynamic were studied from different levels of flow and changes regulation of blood and its components. Studies have shown that malignant tumors have a significant impact on normal blood flow in cancer patients. With the aggravation of tumor severity, the changes of hemodynamic indexes become more and more obvious. With the improvement of the body function of the patients, the related indicators will return to normal level\(^{[14-16]}\). Among them, HR and MAP can reflect whether the patient is in the proper depth of anesthesia and the degree of pain stimulation, which plays an indicative role in maintaining normal perfusion of microcirculation and inhibiting the operation stress response\(^{[17]}\). The results show that, compared with before the induction of anesthesia, HR levels were significantly increased after operation 6h in the two groups \((P<0.05)\), MAP level of postoperative 6 h in the control group was significantly increased \((P<0.05)\) and the change of MAP level in the observe group is not obvious \((P>0.05)\). Compared with the control group, the levels of HR and MAP in the observation group after 6 h were significantly lower than those in the control group \((P<0.05)\). The hemodynamic state of the observation group was more stable than that of the control group. It may be that dexmedetomidine can exert a significant sedative effect on the body and maintain the stability of the blood microcirculation, thus helping to reduce the heart rate and blood pressure during the operation. Cytokine is an active polypeptide secreted by immune cells, which plays an important role in the regulation of cellular physiological function and the body's trauma\(^{[18]}\). IL-2 is associated with cellular immunity and inflammatory response, and IL-10 is mainly involved in humoral immune process. The decrease of IL-2 level and the increase of IL-10 level are closely related to immunosuppression. CRP is an acute phase response index, which can be significantly increased under acute stress, inflammation and tumor\(^{[18-20]}\). The results of this study showed that compared with before anesthesia induction, the levels of CRP were significantly increased at each time point in the two groups \((P<0.05)\). The level of 24 h in the two groups decreased significantly after operation \((P<0.05)\), but increased at 72 h after operation, and significantly increased compared with that before anesthesia \((P<0.05)\). IL-10 in two groups increased significantly at 6 h after operation \((P<0.05)\), but decreased at 72 h after operation and decreased significantly compared with that before induction \((P<0.05)\). Compared with the control group, the levels of CRP, 72h and IL-10 in the observation group after 6 h, 24 h, 72 h were significantly lower than those in the control group, the level of IL-2 was significantly higher than that of the control group, the differences were statistically significant \((P<0.05)\). The results showed that the two groups of inflammatory factors CRP levels were significantly increased, while the observation group was significantly lower than the control group, indicating that the operation will cause inflammation in patients, and the control group inflammatory reaction is more obvious. The initial IL-10 level increased significantly after surgery in two groups, IL-2 levels were significantly lower, but after 72 the level of response, and the observation group was significantly higher than that recovery, the observation group of the inflammation effect is more obvious. The mechanism may be that dexmedetomidine can selectively stimulate the -2 adrenal receptor and activate the cholinergic anti-inflammatory pathway, thereby reducing the inflammatory factors and increasing the level of anti-inflammatory cytokines to achieve anti-inflammatory effects.

T lymphocyte level can indicate the cellular immune level, and monitoring the level of tumor cell immune regulation, which is helpful to judge the curative effect and prognosis\(^{[21]}\). CD3’ lymphocyte subsets assist T cells to recognize antigens, and the decrease of their levels suggests that the immune function of the cells is inhibited. CD4’ cells are helper immune cells that help B cells differentiate into antibodies. CD8’ cells are inhibitory immune cells that inhibit the synthesis and secretion of antibodies and reduce the proliferation of T cells. The decrease of CD4’/CD8’ ratio indicates that cellular immunity is inhibited, which is a common index to evaluate immune function\(^{[22,23]}\). The results of this study showed that compared with before anesthesia induction, the levels of CD3’, CD4’ and CD4’/CD8’ in the control group after 6 h, 24 h and 72 h were significantly decreased \((P<0.05)\). In the observation group, the above indexes decreased significantly after 24 h \((P<0.05)\), but recovered at 72 h after operation, and had no obvious change compared with that before anesthesia induction \((P>0.05)\). At the same time, the levels of CD3’, CD4’ and CD4’/CD8’ in the observation group at 6 h, 24 h and 72 h after operation were significantly higher than those in the control group \((P<0.05)\). The results show that the immune function after surgery in the control group at each time point were suppressed, and the observation group in the postoperative 72h level of each index rebounded, and at each time point between the two groups, the observation group of immune inhibition reaction was less than the control group. That dexmedetomidine has significant effect on improving the immune function, which may be the cause of dexmedetomidine can reduce the level of catecholamines and sympathetic nerve activity to inhibit the stress response, to improve immune suppression effect.

In summary, dexmedetomidine assisted anesthesia for elderly patients with gastric cancer can reduce the stress reaction of patients caused by surgical trauma, improve immunity, reduce inflammation, and hemodynamics of patients with perioperative stable effect. It is worthy of clinical promotion.
Reference


