



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

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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 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, and the lower control group E, NE and ET-1 increased, the observation group after 4 h, 12 h, 24 h E, NE, ET-1 lower than that of the control group; compared with T₀, 2 patients in group T₂, T₃ sIL-2R, IL-6, TNF-alpha were increased, the observation group T₂, T₃ sIL-2R, IL-6, TNF- were 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⁺, CD₈⁺, CD₄⁺/CD₈⁺ 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.

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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 induction of the observation group were given dexmedetomidine (Jiangsu Hengrui medicine, Zhunzi H20090248) 0.4 g/kg diluted with saline to 20 mL, the control group was given normal saline 20 mL, 15 min after injection pump. Maintenance of anesthesia: adjusted TCI propofol (plasma target concentration of 4-6 ng/mL), intermittent injection of atracurium 0.03 mg/kg, and maintained BIS at 40-50. Then in the observation group, dexmedetomidine was pumped continuously at 0.4 g/kg·h, and the control group was injected with saline continuously until the operation was over.

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) 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 (TNF- α) level. (2) stress reaction: venous blood was collected at 4 h before and after operation, 12 h after operation, and 24 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. CD₃⁺, CD₄⁺, CD₈⁺ and CD₄⁺/CD₈⁺ were measured by flow cytometry.

2.4 Statistical analysis

The measurement data to ($\bar{x}\pm s$) said, with t test; count data by using the χ^2 test; correlation analysis of NLR, WBC, PCT, hs-CRP using the Spearman rank correlation analysis method; statistical software SPSS 13, $P<0.05$ was statistically significant.

3. Result

3.1. Changes of inflammatory factors at different times

Compared with T₀, the T₂, T₃, sIL-2R, IL-6 and TNF- α in both groups were increased ($P<0.05$), while those of the observation group, T₂ and T₃, sIL-2R, IL-6 and TNF- α , were lower than those in the control group ($P<0.05$) at the same time. See Table 1.

Table 1.

Changes of inflammatory factors at different time

Group	Time	sIL-2R (pg/mL)	IL-6 (pg/mL)	TNF- α (pg/mL)
	T ₀	62.54±5.71	14.54±4.85	17.63±6.23
Observation group	T ₁	73.56±5.74 [#]	27.52±6.81 [#]	35.74±6.13 [#]
	T ₂	76.58±4.95 [#]	34.37±5.74 [#]	38.25±5.12 [#]
	T ₃	77.36±5.29 [#]	31.33±5.41 [#]	36.35±5.57 [#]
Control group	T ₀	63.58±6.25	14.61±5.18	17.71±7.03
	T ₁	104.75±12.78 [*]	41.54±6.85 [*]	57.65±6.81 [*]
	T ₂	107.69±13.84 [*]	45.29±5.74 [*]	65.77±7.45 [*]
	T ₃	108.95±14.36 [*]	48.72±7.38 [*]	68.27±6.92 [*]

Note: compared with the same group ^{*} $P<0.05$, T₀, 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 E, NE, ET-1 lower than that of the control group ($P<0.05$). See table 2.

Table 2.

Changes of stress indexes at different time.

Group	Time	E (ng/L)	NE (ng/L)	ET-1 (ng/L)
Observation group	Preoperative	59.76±15.45	587.36±98.57	141.26±24.36
	4 h postoperatively	60.54±16.28 [#]	475.41±114.37 [#]	143.56±27.37 [#]
	12 h postoperatively	56.78±15.36 [#]	393.78±105.75 [#]	147.37±25.68 [#]
	24 h postoperatively	55.86±14.37 [#]	377.19±95.43 [#]	139.75±23.69 [#]
Control group	Preoperative	58.85±15.23	489.56±102.31	141.38±26.11
	4 h postoperatively	65.71±15.23 [*]	557.45±125.32 [*]	179.63±37.26 [*]
	12 h postoperatively	67.45±15.36 [*]	518.57±102.63 [*]	174.37±26.75 [*]
	24 h postoperatively	63.15±14.62	505.78±103.29 [*]	165.45±29.34 [*]

Note: compared with the same group before operation, ^{*} $P<0.05$, compared with the control group [#] $P<0.05$.

Table 3.

Changes of immune indexes at different time.

Group	Time	CD ₃ ⁺ (%)	CD ₄ ⁺ (%)	CD ₈ ⁺ (%)	CD ₄ ⁺ /CD ₈ ⁺ (%)
Observation group	Preoperative	61.36±5.48	37.23±4.51	32.13±3.41	1.48±0.71
	4 h postoperatively	53.82±7.55 [#]	29.64±5.17 [#]	28.54±3.17 [#]	1.19±0.43 [#]
	12 h postoperatively	48.74±6.75 [#]	26.74±3.46 [#]	26.45±4.07 [#]	1.02±0.35 [#]
	24 h postoperatively	55.71±9.12 [#]	33.41±4.26 [#]	29.25±5.36 [#]	1.32±0.57 [#]
Control group	Preoperative	60.57±5.63	37.31±5.19	33.07±4.02	1.49±0.69
	4 h postoperatively	46.56±6.23 [*]	26.12±5.38 [*]	25.15±4.13 [*]	1.05±0.52 [*]
	12 h postoperatively	44.37±5.65 [*]	24.23±4.38 [*]	22.08±3.16 [*]	0.91±0.27 [*]
	24 h postoperatively	52.70±7.23 [*]	30.68±5.09 [*]	27.27±4.11 [*]	1.21±0.37 [*]

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 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). 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 excitement, 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]. 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.

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[8]. SIL-2R is a low affinity receptor, mainly derived from activated T lymphocyte membrane receptor protein on the cell membrane, and sIL-2R combined with IL-2, the proliferation and function of immune cells, inhibit tumor cell division and proliferation, thereby inhibiting the immune response[9]. 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[10]. TNF-alpha is a cytokine with dual biological effects, such as anti-infective, anti tumour 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[11]. The study confirmed that[12], 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 reduce the production of inflammatory cytokines. Some scholars of dexmedetomidine combined with ulinastatin on elderly patients with colorectal cancer control 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[13]. This study shows that, compared with T₀, 2 patients in group T₂, T₃ sIL-2R, IL-6, TNF-alpha were increased (*P*<0.05), the observation group T₂, T₃ sIL-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 CD_3^+ , CD_4^+ , CD_8^+ and CD_4^+/CD_8^+ decreased ($P<0.05$), the observation group after 4 h, 12 h, 24 h CD_3^+ , CD_4^+ , CD_8^+ , CD_4^+/CD_8^+ 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

- [1] Huang Yong, Zhu Xuanjin, Liu Jianwei. Safety of laparoscopic surgery for elderly patients with colorectal cancer. *J Pract Med* 2015; **31**(4): 556-558
- [2] Zhang Weihua. Continuous infusion of dexmedetomidine on hemodynamics in patients undergoing laparoscopic surgery and anesthesia affects the quality. *Modern Pract Med* 2015; **27**(12): 1605-1607
- [3] Lin Fusen, Liao Xiqiang, Lu Guiming. Strengthen the perioperative management of elderly patients with postoperative complications of laparoscopic surgery on. *Clin Med Eng* 2015; **22**(1): 43-44
- [4] Zheng Jing, Zhang Hongqin, Zhang Jin. Effects of dexmedetomidine on inflammatory factors and early cognitive function in elderly patients undergoing laparoscopic surgery. *Clin Rational Use Drugs* 2016; **9**(1C): 19-21
- [5] Xu Xiaoyan, Wu Wei. The influence of dexmedetomidine on hemodynamics and stress response during gynecological laparoscopic surgery. *Sichuan Med Univ* 2016; **37**(1): 70-73
- [6] Hoffman J, Hamner C. Effectiveness of dexmedetomidine use in general anesthesia to prevent postoperative shivering: a systematic review protocol. *JBI Database System Rev Implement Rep* 2015; **13**(2): 37-48
- [7] Wu Dafeng, Lu Liang, Li Sijuan. The effect of dexmedetomidine on general anesthesia in elderly patients with cardiovascular disease in lower abdominal surgery anesthesia hemodynamics during recovery period. *Cardiovascular Dis Prevent Control* 2016; **16**(6): 462-464
- [8] Tong Kai. Effects of different doses of dexmedetomidine on agitation and early cognitive function in laparoscopic colorectal cancer surgery. *Chin J Endoscopy* 2015; **21**(4): 356-359.
- [9] Deng Aiqin, Deng Zhilian, Xu Lin. Effects of different doses of dexmedetomidine on inflammatory factors in patients undergoing laparoscopic surgery for uterine malignancies. *Guangdong Med Univ* 2016; **37**(10): 1549-1551
- [10]Feng Yanling, Yang Xiaolei, Qian Xiao Min. Different doses of dexmedetomidine on laparoscopic cholecystectomy on cognitive function and inflammatory factors in elderly patients. *Modern Med* 2016; **44**(11): 1499-1530
- [11]Zheng Xiangli, Zhang Mei, Yang Zhanmin. Effects of different doses of dexmedetomidine on postoperative acute phase in elderly patients. *J Hainan Med Univ* 2016; **22**(10): 1037-1040
- [12]Huang Qiaowen, Cai Lisheng. The effect of dexmedetomidine on cytokines in elderly patients under general anesthesia during laparoscopic colorectal surgery stress levels and postoperative effect. *Chin Clin Pharmacol Ther* 2016; **21**(7): 802-805
- [13]Pan Changling, Chen Yi, Wu Yuehong. The effects of dexmedetomidine combined with ulinastatin on regulation of proinflammatory/anti-inflammatory system to improve the elderly patients with colorectal cancer postoperative cognitive dysfunction in the effect. *World J Gastroenterol* 2016; **24**(17): 2755-2761
- [14]Wang Hongzhi, Han Chongfang. Influence of dexmedetomidine on perioperative immune function in elderly patients undergoing radical resection of lung cancer. *Chin Med Clin* 2014; **14**(9): 1274-1275
- [15]Zhou Ruhong, Li Hong, Zhang Xu. The effects of different doses of dexmedetomidine on the immune function and stress response during the recovery stage in elderly patients with lung cancer. *Med Rev* 2016; **22**(7): 1394-1397
- [16]Pi Zhibing, Lin hai, Xu Xuzhong. Effect of different doses of dexmedetomidine on analgesia and stress and immune function in elderly patients undergoing laparoscopic surgery. *Chin J Clin Pharmacol* 2015; **31**(17): 1709-1712