

## **Influence of dexmedetomidine on stress level and postoperative cytokines of laparoscopic operation for colorectal cancer of senile patients with general anesthesia.**

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### **Abstract**

**Purpose:** It aims to explore the influence of dexmedetomidine on stress level and postoperative cytokines of laparoscopic operation for colorectal cancer of senile patients with general anesthesia.

**Method:** 60 cases of patients of 65-80 y old with ASA levels of I-II who are planned to be conducted with laparoscopic operation for colorectal cancer are selected and divided into the Dexmedetomidine group and the saline group, 30 cases for each group. The patients of the dexmedetomidine group are injected with Dexmedetomidine of 0.4 µg/kg with venous pumps before anesthesia induction within 10 min, and Dexmedetomidine of 0.4 µg•kg<sup>-1</sup>•h<sup>-1</sup> is in combined during maintenance of anesthesia. The patients of the saline group are applied with normal saline of equivalent quantity. The Mean Arterial Pressure (MAP), Heart Rate (HR) and Cortisol (Cor) are recorded at entrance (T0), after injection of dexmedetomidine (T1), immediately after the tracheal intubation (T2), pneumoperitoneum (T3) and immediately after tracheal extubation (T4); the interleukin-6 (IL-6) and interleukin-10 (IL-10) at T0, T4, 24 h after operation (T5) and 48 h after operation (T6) are also recorded.

**Results:** The MAP and HR levels of the dexmedetomidine group at T1-4 are significantly lower than that of the saline group (P<0.05); the Cor level of the Dexmedetomidine group at T2-4 is significantly lower than that of the saline group (P<0.05); the IL-6 level of the dexmedetomidine group at T4-6 is significantly lower than that of the saline group (P<0.05); the IL-10 level of the dexmedetomidine group at T4-6 is significantly lower than that of the saline group (P<0.05).

**Conclusion:** Dexmedetomidine can be applied to laparoscopic operation for colorectal cancer of senile patients with general anesthesia, which is beneficial to the relieving of stress response by reducing the release of Cor; in addition, it helps relieve the release of the proinflammatory factor IL-6 and increase that of the postoperative anti-inflammatory factor IL-10, maintaining the balance of cytokines.

**Keywords:** Dexmedetomidine, Senile patients, Stress, Interfeukin-6, Interfeukin-10.

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### **Introduction**

Laparoscopic operation for colorectal cancer may induce intra-abdominal hypertension and hypercapnia due to pneumoperitoneum, giving rise to strong stress response, which may lead to changes of neuroendocrine and immune system of human bodies. It may result in changes on levels of hormones such as Cortisol (Cor) and many cytokines, giving rise to inflammatory response, adverse to the recovery of patients. As an efficient and highly selective α<sub>2</sub>-receptor stimulant, Dexmedetomidine is widely applied to surgery anesthesia to relieve stress in operations, so as to adjust the inflammatory level which has been reported in literatures in recent years [1]. By observing the influence of dexmedetomidine on stress level and postoperative cytokines of laparoscopic operation for colorectal cancer of senile patients, this research provides references for applications of

dexmedetomidine in general anesthesia in senile cancer patients.

### **Data and Method**

#### ***Patients and groups***

The research was conducted after the approval of the Ethics Committee of the hospital, with signatures on Informed Consent by the patients and their relatives. 60 cases of patients with ages of 65-80 y old of ASA I-II levels to be conducted with laparoscopic operation for colorectal cancer were divided into the Dexmedetomidine group and the saline group randomly, 30 cases in each group. All the patients had no concurrent infection, fever, autoimmune disease, endocrine metabolic disease, hypertension, bradycardia or

atrioventricular block, or history of  $\beta$ -blocker and  $\alpha_2$ -receptor stimulant taking.

### Anesthesia method

The dexmedetomidine was prepared as per the stipulation of 4  $\mu\text{g}/\text{ml}$ , which was infused at the load dosage of 0.4  $\mu\text{g}/\text{kg}$  at constant speed 10 min before anesthesia induction; the dexmedetomidine of 0.4  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$  was combined during maintenance of anesthesia. The patients of the saline group were applied with normal saline with the same volume at the same time. The propofol of 1.5  $\text{mg}/\text{kg}$ , the sufentanil of 0.4  $\mu\text{g}/\text{kg}$  and the cisatracurium besylate of 0.2  $\text{mg}/\text{kg}$  were adopted for anesthesia induction. The trachea incubation was conducted 3 minutes after the induction for mechanical ventilation. The propofol of 4-12  $\text{mg}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ , the remifentanil of 0.05-0.3  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  and the cisatracurium besylate were conducted with pump intravenous as maintenance of anesthesia during operation. The blood pressure of the patients of maintenance during operation was kept within  $\pm 30\%$  of that before operation. The infusion of dexmedetomidine or saline and cisatracurium besylate of both of the two groups was stopped 40 min before the end of the operation. They were applied with sufentanil of 0.1  $\mu\text{g}/\text{kg}$  30 min before the end of the operation. The infusion of propofol and remifentanil was stopped at the end of pneumoperitoneum. The same automatic control venous analgesia method was applied to both of the two groups after operation.

### Monitoring of observation indexes and recording of the entering of the two groups

The MAP, HR and Cor levels at (T0), after the injection of Dexmedetomidine of load dosage (T1), immediately after the tracheal intubation (T2), pneumoperitoneum (T3) and immediately after tracheal extubation (T4) were recorded; the

IL-6 and IL-10 at T0, T4, 24 h after operation (T5) and 48h after operation (T6) were measured with ELISA.

### Statistical processing

The SPSS 19.0 statistical software was adopted for analysis in statistics. The measurement data was expressed with mean value  $\pm$  standard deviation ( $\bar{x} \pm s$ ). The repeated measured and designed variance analysis was adopted for comparisons of MAP, HR, Cor, IL-6 and IL-10. The Dunnett's T3 test was then adopted for comparisons among groups at different points of time. The difference has statistical significance if  $P < 0.05$ .

## Results

### General conditions of the patients

There were no statistical difference on age, body mass, operation time and amount of bleeding between two groups ( $P > 0.05$ , Table 1).

### The MAP, HR and Cor levels of the two groups

The MAP and HR levels of the Dexmedetomidine group were significantly lower than that of the saline group at T1-4 ( $P < 0.05$ ). The serum Cor level of the Dexmedetomidine group was significantly lower than that of the saline group at T2-4 ( $P < 0.05$ , Table 2).

### The IL-6 and IL-10 levels after operation

The serum IL-6 level of the dexmedetomidine group at T4-6 was significantly lower than that of the saline group, and the IL-10 level was significantly higher than that of the saline group ( $P < 0.05$ , Table 3).

**Table 1.** General conditions of the patients of the two groups ( $\bar{x} \pm s$ ,  $n=30$ ).

Group	Age (years old)	Body mass (kg)	Operation time (min)	Amount of bleeding (ml)
Dexmedetomidine group	69.5 $\pm$ 4.2	60.3 $\pm$ 5.9	133 $\pm$ 31	59 $\pm$ 31
Saline group	67.8 $\pm$ 4.3	62.7 $\pm$ 5.5	125 $\pm$ 26	62 $\pm$ 28

**Table 2.** MAP, HR and Cor levels of the two groups at different time ( $\bar{x} \pm s$ ,  $n=30$ ).

Group	Index	T0	T1	T2	T3	T4
Dexmedetomidine group	MAP (mmHg)	96.1 $\pm$ 8.0	86.1 $\pm$ 9.3 <sup>b</sup>	102.3 $\pm$ 9.2 <sup>b</sup>	91.6 $\pm$ 6.6 <sup>b</sup>	97.7 $\pm$ 7.9 <sup>b</sup>
	HR (bpm)	75.2 $\pm$ 8.8	63.4 $\pm$ 8.4 <sup>b</sup>	73.8 $\pm$ 6.0 <sup>b</sup>	71.9 $\pm$ 7.9 <sup>b</sup>	75.2 $\pm$ 8.2 <sup>b</sup>
	Cor (ng/ml)	193.2 $\pm$ 25.7	191.8 $\pm$ 21.6	197.1 $\pm$ 38.8 <sup>b</sup>	240.8 $\pm$ 26.3 <sup>b</sup>	245.7 $\pm$ 24.7 <sup>b</sup>
Saline group	MAP (mmHg)	94.0 $\pm$ 9.0	98.2 $\pm$ 7.0	110.2 $\pm$ 6.1	110.9 $\pm$ 10.7	109.2 $\pm$ 8.5
	HR (bpm)	74.9 $\pm$ 8.0	73.1 $\pm$ 7.4	83.9 $\pm$ 9.8	83.0 $\pm$ 9.1	85.9 $\pm$ 8.8
	Cor (ng/ml)	196.7 $\pm$ 25.9	196.3 $\pm$ 25.6	224.6 $\pm$ 19.5	271.2 $\pm$ 24.9	357.3 $\pm$ 32.8

$P < 0.05$  when compared with that of the saline group.

**Table 3.** Comparisons on serum IL-6 and IL-10 levels of the two groups at different time ( $\bar{x} \pm s$ , n=30).

Group	Index	T0	T4	T5	T6
Dexmedetomidine group	IL-6 (pg/ml)	43.9 ± 5.4	67.5 ± 9.2 <sup>b</sup>	58.2 ± 4.9 <sup>b</sup>	52.1 ± 3.0 <sup>b</sup>
	IL-10 (pg/ml)	14.5 ± 1.7	58.8 ± 4.3 <sup>b</sup>	49.4 ± 8.0 <sup>b</sup>	20.8 ± 3.1 <sup>b</sup>
Saline group	IL-6 (pg/ml)	46.5 ± 5.6	80.9 ± 15.2	65.3 ± 6.7	60.8 ± 3.9
	IL-10 (pg/ml)	14.3 ± 1.7	46.6 ± 4.5	38.2 ± 3.3	17.6 ± 2.0

P<0.05 when compared with the saline group

## Discussion

As the information molecules mediating immune and inflammatory response, cytokines can be divided into inflammatory cytokines and anti-inflammatory cytokines, represented by IL-6 and IL-10, respectively, which maintain the balance of cytokines *in vivo* [2]. Considering the reduced immunity of senile cancer patients, the strong stress response during the perioperative period destroys the balance of postoperative cytokines of cancer patients and disturbs their immune system. In this research, at time points with large simulation of the anesthesia and operation such as T2, T3 and T4, the MAP, HR and Cor levels of the Dexmedetomidine group are significantly reduced when compared with the saline group, indicating that the patients of the dexmedetomidine group have weaker stress response level to trachea incubation, extubation and pneumoperitoneum. It is consistent with the research findings of Sulaiman [3] and Li [4]. It is because by combining with the central and peripheral  $\alpha_2$ -receptors, dexmedetomidine restrains the activity of sympathetic nerves, giving rise to decline on blood pressure and heart rate. The serum IL-6 level of the patients of the dexmedetomidine group in this research is significantly lower than that of the saline group while the IL-10 level of the patients of the dexmedetomidine group is significantly higher than that of the saline group. It indicates that dexmedetomidine restrains the release of IL-6 and that of IL-10. Large quantities of experimental researches and clinical researches also prove the anti-inflammatory effect of dexmedetomidine, which may be associated with the activation of the anti-inflammatory access of cholinergic by restraining the sympathetic activity or excites the imidazoline receptors for anti-inflammatory action, or its reduction on generation of inflammatory factors by regulating

nuclear factor-kB. In general, dexmedetomidine can be applied to laparoscopic operation for colorectal cancer of senile patients with general anesthesia, which not only restrains the stress response in operation but also contributes to postoperative balance of cytokines.

## References

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