EFFECTS OF DIFFERENT DOSES OF DEXMEDETOMIDINE IN PATIENTS WITH COLORECTAL CANCER

YUHUA KONG[1,#], ZHUOYA BAI[1,#], LIN CHEN[2], YONGLING YAO[3,*]
[1]Department of Anesthesiology, Xiangyang No.1 People's Hospital, Hubei University of Medicine, Xiangyang, 322200, China - [2]Department of Urinary surgery, Xiangyang No.1 People's Hospital, Hubei University of Medicine, Xiangyang, 322200, China - [3]Department ofPain, Xiangyang No.1 People's Hospital, Hubei University of Medicine, Xiangyang, 322200, China
[#]*The first two authors contributed equally to this paper*

ABSTRACT

Objective: *To explore the effects of different doses of dexmedetomidine (DEX) on emergence agitation after anesthesia and postoperative pain in colorectal cancer (CRC) patients after radical resection.*

Methods: *A total of 180 CRC patients undergoing radical resection treated in our hospital from January 2019 to January 2020 were selected as the research objects and divided into group A (n=60), group B (n=60) and group C (n=60)based on the administration method. Groups A and B were given 0.4 μg•kg-1 and 0.8 μg•kg-1DEX respectively with pump injection during anesthesia induction and group C was injected with the same amount of normal saline to compare their agitation scores, sedation scores, inflammatory factor levels, recovery time, postoperative pain scores and incidences of adverse reactions.*

Results: *Compared with group C, groups A and B achieved significantly lower agitation scores (P<0.001) and significantly higher sedation scores (P<0.001), and the sedation score of group A was significantly lower than that of group B (P<0.001); group A and group B showed significantly higherintraoperative and wake-up levels of interleukin 10 (IL-10) (P<0.001) and significantly lower levels of tumor necrosis factor (TNF-α) and C-reactive protein (CRP) (P<0.001) than Group C; between group A and group B, the level of IL-10 was significantly lower (P<0.001) and the levels of TNF-α and CRP were significantly higher in group A (P<0.001); the recovery time of group A was significantly shorter than that of groups B and C (P<0.001);groups A and B achieved significantly lower postoperative pain scores than group C (P<0.05); and groups A and C achieved significantly lower incidences of adverse reactions compared with group B (P<0.05).*

Conclusion: *For patients undergoing radical resection of colorectal cancer, 0.4 μg•kg-1 DEX can ease the emergence agitation after anesthesia, improve the inflammatory factor level, alleviatethe postoperative pain, and lower the possibility of adverse reactions, which should be promoted and applied.*

Keywords: *Dexmedetomidine, colorectal cancer, emergence agitation.*

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Introduction

Radical resection of colorectal cancer (CRC) involves wide scope of resection, more traction from patients' body tissues, easy occurrence of perioperative stress response, and difficulty in recovery from anesthesia, and even if patients recover smoothly, they may feel intense postoperative pain that seriously affects the recovery process[1-3]. Patient controlled analgesia (PCA)is an important way to reduce the postoperative pain, but high doses of drugs can cause adverse effects.Study on reducing the likelihood of emergence agitation (EA) after anesthesia and alleviating the postoperative pain is a high priority in the clinical anesthesia research[4-7]. As a novel adrenergic receptor agonist, dexmedetomidine (DEX) can weaken the intraoperative stress, relieve the EA response, and then reduce problems such as rupture wounds caused by severe agitation for patients.Previous studies

have confirmed that DEX pretreatment can improve perioperative stress response in patients undergoing radical hysterectomy for endometrial carcinoma[8-11], but there are very few theoretical studies that apply it to the radical resection of CRC.

Based on this, to explore the effects of different doses of DEX on emergence agitation after anesthesia and postoperative pain in CRC patients after radical resection, a total of 180 patients admitted to our hospital from January 2019 to January 2020 were selected for the study, and the summary results are as follows.

Materials and methods

General data

A total of 180 CRC patients undergoing radical resection admitted to our hospital from January 2019 to January 2020 were selected for the study and divided into group A (n=60), group B (n=60) and group C (n=60), with no statistical difference in the patients' general data of the three groups (P>0.05), see Table 1. The study was approved by the Hospital Ethics Committee.

Group	N	Age (year)	Weight (kg)	Anesthesia grade (case)		Disease type (case)	
				I	II	Colon cancer	Rectal cancer
Group A	60	64.89±5.26	62.12±6.21	28	32	35	25
Group B	60	65.01±5.24	62.14±6.23	29	31	34	26
Group C	60	64.99±5.32	62.10±6.25	30	30	36	24

Table 1: Comparison of patients' general data.

Inclusion criteria

The inclusion criteria for this study were as follows:

• Patients or their family members fully understood the research process and signed the informed consent;

• Patients were diagnosed with colorectal cancer by examination[12];

• The anesthesia grades were I-II[13];

• The radical resection of colorectal cancer was required.

Exclusion criteria

The exclusion criteria for the patients in this study were as follows:

• Presence of mental problems or inability to communicate with others;

• Suffering from other organic diseases;

• Allergy to DEX;

• Presence of surgical contraindications[14];

• Use of anticoagulant within the month prior to the study[15];

• Abdominal skin infection.

Methods

Group A and group B were given 0.4 μg•kg-1 and 0.8 μg•kg-1DEX respectively with pump injection during anesthesia induction and group C was injected with the same amount of normal saline, with the following specific steps;

• After entering the operating room, all patients' peripheral vein passages and invasive arterial pressure were established, and routine ECG monitoring and oxygen inhalation were performed;

• Before anesthesia induction, group A and group B were given 0.5 μg·kg-1DEX (Cisen Pharmaceutical Co., Ltd., SFDA approval no.H20130027) respectively in advance, and group C was injected with the same amount of normal saline;

• After anesthesia induction and tracheal intubation, group A and group B were given 0.4 μg•kg-1 and 0.8 μg•kg-1DEX respectively with pump injection (stopped at 0.5h before the operation), and Group C was injected with the same amount of normal saline at the same time;

• Propofol (Jiangsu Nhwa Pharmaceutical Co., Ltd.; SFDA approval no. H20123138) and sufentanil (Yichang Humanwell Pharmaceutical Co., Ltd.; SFDA approval no.H20054171) were selected for anesthesia maintenance, and vecuronium (Nanjing Xinbai Pharmaceutical Co., Ltd.; SFDA approval no. H20067267) was added for every 0.5h;

• Disposable intravenous analgesia pump was used after the operation.

Observation criteria

• Agitation score. A score of 0 was considered that the patient was quiet and cooperative; a score of 1 was considered that the patient complained of discomfort when questioned, but had no behavioral response; a score of 2 was considered that the patient frequently complained of discomfort; and a score of 3 was considered that the patient had behavioral responses such as moving hands or feet[16].

• Sedation score. Based on the Ramsay Sedation Scale, a score of 1 indicated that the patient was restless;a score of 2 indicatedthat the patient was quiet and cooperative; a score of 3 indicatedthat the patient was lethargic but following instructions;a score of 4 indicatedthat the patient was in sleep and arousable; a

score of 5 indicatedthat the patient was unresponsive to call; and a score of 6 indicatedthat the patient was deeply asleep and unable to awaken[17].

• Inflammatory factor levels. Patients' IL-10, TNF-α and CRP levels were compared before the operation, during the operation and in the recovery period.

• Recovery time. Patients' breathing recovery time, time of eye-opening on calling and extubation time were compared.

• Postoperative pain score. Based on the visual analogue scale (VAS) for pain, the score was ranged from 0 to 10, with higher scores indicating greater pain. The time nodes for comparison were 2h, 8h and 24h after the operation[18].

• Incidence of adverse reactions. The adverse reactions included arrhythmia, hypertension, bradycardia, and nausea and vomiting, and the number of patients with such reactions was counted.

Statistical processing

In this study, the data processing software was SPSS20.0, the picture drawing software was GraphPad Prism 7 (GraphPad Software, San Diego, USA), items included were enumeration data and measurement data, methods used were X^2 test and t-test, and differences were considered statistically significant at $P<0.05$.

Results

Comparison of patients' agitation scores

Groups A and B achieved significantly lower agitation scores than group C ($P<0.001$), but there was no statistical difference between group A and group B ($P>0.05$), see Figure 1.

Comparison of patients' sedation scores

In terms of the sedation score, group A and group B were significantly higher than group C ($P<0.001$), and group A was significantly lower than group B ($P<0.001$), see Figure 2.

Comparison of patients' inflammatory factor levels

Compared with group C, group A and group B achieved significantly higher IL-10 level in the recovery period ($P<0.001$) and significantly lower TNF-α and CRP levels ($P<0.001$); and compared with group B, group A achieved significantly lower IL-10 level ($P<0.001$) and significantly higher TNF-α and CRP levels ($P<0.001$), see Table 2.

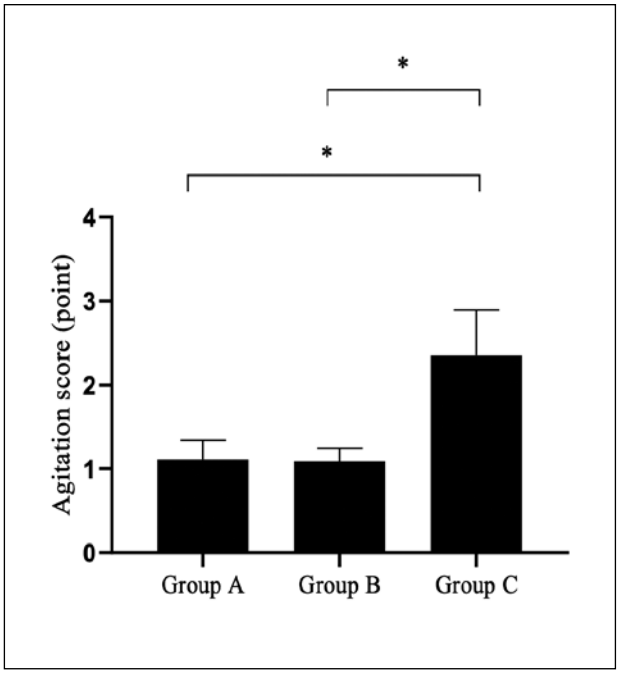

Figure 1: Comparison of patients' agitation scores ($\bar{x}\pm s$, point).

*Note: In Figure 1, the horizontal axis from left to right showed the group A, group B and group C, and the vertical axis showed the agitation score (point). The agitation scores of groups A, B and C were (1.11±0.23) points, (1.09±0.15) points and (2.35±0.54) points, respectively. *meant P<0.001.*

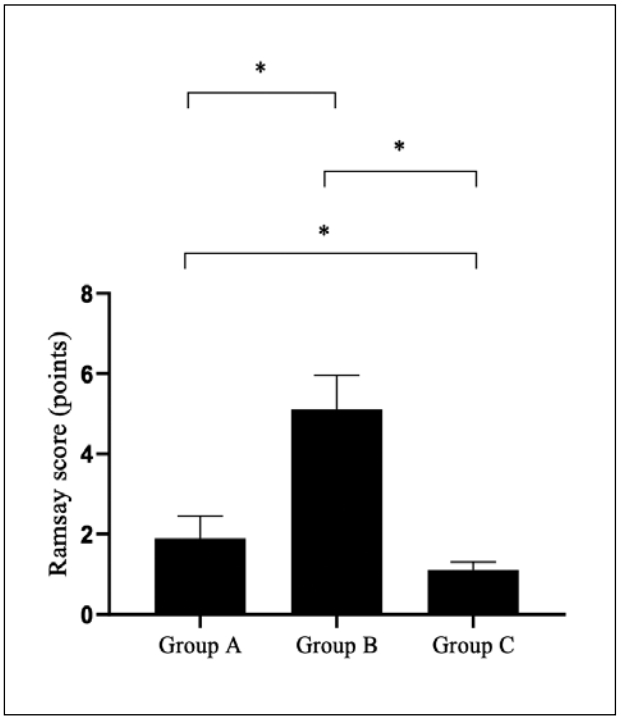

Figure 2: Comparison of patients' sedation scores ($\bar{x}\pm s$, point).

*Note: In Figure 2, the horizontal axis from left to right showed the group A, group B and group C, and the vertical axis showed the Ramsay score (point). The sedation scores of groups A, B and C were (1.89±0.56) points, (5.11±0.85) points and (1.10±0.20) points, respectively. *meant P<0.001.*

Group	IL-10 (pg/L)			TNF-α (pg/L)			CRP (mg/L)		
	Preoperative	Intraoperative	Wake-up	Preoperative	Intraoperative	Wake-up	Preoperative	Intraoperative	Wake-up
Group A	12.15±1.65	23.56±2.15*	25.68±2.65*	18.99±1.20	22.57±1.65*#	30.59±1.85*#	12.10±0.65	23.15±2.54*#	41.11±3.25*#
Group B	12.21±1.56	24.11±2.31*	25.98±2.65*	18.98±1.51	19.56±1.34*	22.11±1.87*	12.05±0.65	19.12±1.68*	19.65±2.65*
Group C	12.56±1.76	16.54±2.10	18.66±2.15	18.99±1.02	34.25±2.56	51.69±3.65	12.15±0.36	35.98±3.24	65.12±4.26

Table 2: Comparison of patients' inflammatory factor levels ($\bar{x}\pm s$).
*Note: *indicated that P<0.05 when comparing with group C; #indicated that P<0.05 when comparing with group B.*

Comparison of patients' recovery time

The recovery time of group A was significantly shorter than that of group B and group C (P<0.001), and that of group B was significantly longer than that of group C (P<0.001), see Table 3.

Group	Breathing recovery time	Time of eye-opening on calling	Extubation time
Group A	3.65±0.35*#	4.21±0.65*#	5.00±0.68*#
Group B	7.52±0.35*	11.56±1.21*	13.10±1.35*
Group C	6.32±0.56	9.10±0.87	10.56±1.32

Table 3: Comparison of patients' recovery time ($\bar{x}\pm s$, min).
*Note: *indicated P<0.05 when comparing with group C; #indicated P<0.05 when comparing with group B.*

Comparison of patients' postoperative pain scores

The postoperative pain scores of group A and group B were significantly lower than those of group C (P<0.05), but there was no statistical difference between group A and group B (P>0.05), see Figure 3.

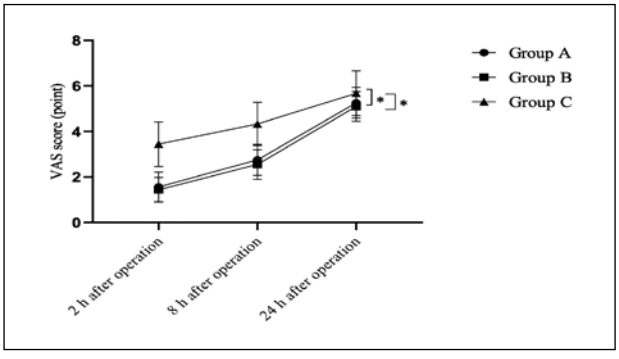

Figure 3: Comparison of patients' postoperative pain scores ($\bar{x}\pm s$, point).
*Note: In Figure 3, the horizontal axis from left to right showed the time points of 2h, 8h and 24h after operation, and the vertical axis showed the VAS score (point); the dot line showed group A, the block line showed group B, and the triangle line showed group C. The VAS scores at 2h after operation of group A, group B and group C were (1.56±0.65) points, (1.44±0.54) points and (3.44±0.98) points, respectively; The VAS scores at 8h after operation of group A, group B and group C were (2.75±0.68) points, (2.55±0.65) points and (4.33±0.95) points, respectively; The VAS scores at 24h after operation of group A, group B and group C were (5.26±0.68) points, (5.10±0.65) points and (5.68±0.98) points, respectively; *meant P<0.05.*

Comparison of patients' incidences of adverse reactions

The incidences of adverse reactions of group A and group B were significantly lower than those of group B (P<0.05), with no statistical difference between group A and group C (P>0.05), see Figure 4.

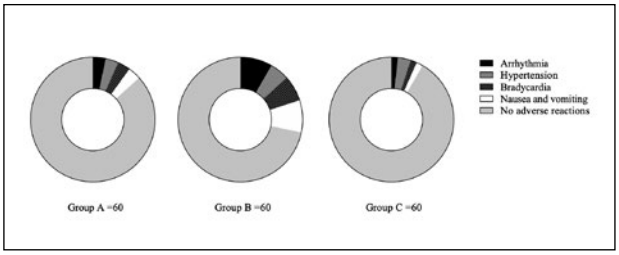

Figure 4: Comparison of patients' incidences of adverse reactions.
Note: In Figure 4, the black area showed arrhythmia, the dark gray area showed hypertension, the black grid area showed bradycardia, the white area showed nausea and vomiting, and the light gray area showed no adverse reactions; the left image showed group A, the middle image showed group B, and the right image showed group C. Two patients in group A, five patients in group B and one patient in group C had arrhythmia; Two patients in group A, three patients in group B and two patients in group C had hypertension; Two patients in group A, four patients in group B and one patient in group C had bradycardia; Two patients in group A, five patients in group B and one patient in group C had nausea and vomiting; and Fifty-two patients in group A, forty-three patients in group B and fifty-five patients in group C had no adverse reactions.

Discussion

EA is a common clinical phenomenon. Most patients experience a vigorous agitated reaction in the first half-hour after operation, which can lead to rupture wound and abnormal hemodynamics and compromise their body health.At present, the academic community has not clarified the mechanism of EA, but it may be related to anesthesia induction, anesthesia maintenance, postoperative analgesia and other factors[19-22]. Reducing the possibility of EA has always been the focus of anesthesia related research. In previous practice, drugs such as tramadol were commonly used for analgesia, but the effect was little and patients were

prone to delayed emergence and other conditions, indicating its limited clinical application. As peoples perception of anesthesia continues to deepen, DEX is gradually applied in practice, for it can relieve patients' central sympathetic nerve impulse and elevate the mobility of the vagus nerve, and thus plays an ideal role of central sedation[23-24]. No uniform conclusion regarding the optimal dose of DEX has been reached in academia. This study showed that in terms of the sedation score, group A and group B were significantly higher than group C (P<0.001), and group A was significantly lower than group B (P<0.001), indicating that there is a more desirable sedation effect of DEX and that the high dose works better than the medium dose. However, the recovery time of group A was significantly shorter than that of group B and group C (P<0.001), and that of group B was significantly longer than that of group C (P<0.001), showing that high-dose DEX would put patients into deep sleep with difficulty in recovery and high drug dependency, so high-dose DEX should be used with caution.

The agitation scores of groups A and B were significantly lower than those of group C (P<0.001), but there was no statistically significant difference between group A and group B (P>0.05), indicating that medium-dose DEX is the optimal sedative drug to avoid drug dependency while sedating patients' central nervous system and relieving EA, which provides a good basis for smooth extubation. In scholar Sato K's research, 0.4 μg•kg-1and 0.8 μg•kg-1 DEX were respectively given to the group A and group B in advance, and the same amount of normal saline was given to the group C, and the agitation scores of group A, group B and group C were (1.21±0.20) points, (1.16±0.10) points and (2.45±0.51) points respectively[25], showing that there was no significant difference between the the sedation effects of medium-dose and high-dose DEX. In addition to agitation scores, inflammatory factors can also reflect patients' agitation condition, an excessive level of inflammatory factors is the key element that leads to EA in patients.

This study showed that compared with group C, patients in group A and group B presented significantly higher intraoperative and wake-up IL-10 levels (P<0.001) and significantly lower TNF-αand CRP levels (P<0.001);between group A and group B, group A achieved significantly lower IL-10 level(P<0.001) and significantly higher TNF-αand CRP levels(P<0.001), suggesting that medium-dose DEX can exert more desirable anti-inflammatory effects and protect the brain function of patients with little negative effect on patient's body tissue, which is more ideal in application.

This study also concluded that the postoperative pain scores of groups A and B were significantly lower than those of group C (P<0.001), with no statistical difference between groups A and B (P>0.05), indicating that the higher the dose of DEX, the less postoperative pain patients are likely to experience due to the fact that DEX inhibits sympathetic nerve impulses. However, too high a dose of DEX will not only cause delayed recovery but also increase the possibility of adverse effects in patients, so the medium dose of DEX should be selected as an anesthetic drug in the clinic to avoid conditions such as nausea and vomiting in patients.

In summary, 0.4μg•kg-1 DEX is able to attenuate emergence agitation after anesthesia, improve the inflammatory factor level, alleviate the postoperative pain, and reduce the possibility of adverse reactions for patients with colorectal cancer undergoing radical surgery, which should be promoted and applied.

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Corresponding Author:
Yongling Yao
Department of Pain, Xiangyang No.1 People's Hospital, No.75 Jiefang Road, Fancheng District, Xiangyang, 322200, China
Email: Yuguan-zhang2021@163.com
(China)