



The Anti-inflammatory Effect of Dexmedetomidine Administration on Patients Undergoing Intestinal Surgery: A Randomized Study

Rushuang Chen¹ · Zhenming Kang¹ · Yaduan Wang¹ · Jie Zhao¹ · Shunyuan Li¹

Accepted: 8 October 2021 / Published online: 9 November 2021
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Abstract

Background and Objective Dexmedetomidine is a highly selective α_2 -adrenergic receptor agonist with sedative, analgesic, anti-sympathetic and stress-reducing effects. It has been widely used as an adjunct for general anesthesia of multiple surgeries. However, the relationship between the utilization of dexmedetomidine in intestinal surgery and the postoperative inflammatory response of patients remains unclear.

Methods A randomized, controlled, single-blinded clinical trial was performed. Eighty-six patients assigned for intestinal surgery were recruited and were randomly divided into two groups (dexmedetomidine group, $n = 40$; control group, $n = 40$) [six participants were excluded due to multiple reasons, such as allergy and drug use history]. The clinical characteristics and physiological outcomes of participants who received different treatments (dexmedetomidine and 0.9% sodium chloride) were collected and analyzed. Blood samples of the two groups were collected before administration (T0), 10 min after pumping dexmedetomidine/saline solution (T1), immediately after the operation started (T2), 30 min after the operation started (T3), and immediately after the operation ended (T4). Enzyme-linked immunosorbent assay (ELISA) was performed to evaluate the proinflammatory factors.

Results Intravenous injection of dexmedetomidine before intestinal surgery decreased a variety of circulating proinflammatory factors. Dexmedetomidine alleviated the stress response and promoted the recovery of cognitive ability among patients undergoing intestinal surgery.

Conclusion Dexmedetomidine administration in patients undergoing intestinal surgery inhibited the surgery-induced inflammatory reactions.

Key Points

Intravenous injection of dexmedetomidine before intestinal surgery reduces multiple circulating proinflammatory factors in patients' serum.

Dexmedetomidine alleviated the stress response and promoted the recovery of cognitive ability among patients undergoing intestinal surgery.

1 Introduction

The intestine is the organ with the largest surface area in the human body [1]. The intestinal mucosa damaged by surgery induces the production of a variety of proinflammatory factors, which leads to the activation of inflammatory cells and the release of multiple inflammatory mediators [2]. The inflammatory reaction caused by intestinal surgery can inhibit intestinal bacteria from invading peripheral blood and distance organs through the damaged intestinal mucosa [3]; however, excessive intestinal inflammation leads to damage and atrophy of intestinal mucosa, and thus decreases its barrier function [4, 5]. A large number of proinflammatory factors released by intestinal tissues can cause systemic inflammatory reactions, resulting in fever, peripheral blood leukocyte alteration, and impaired function of organs such as liver and kidney [6–8]. Therefore, controlling the intraoperative and postoperative inflammatory response of patients with bowel surgery and reducing the secretion of inflammatory factors

✉ Zhenming Kang
kzm991041@163.com

✉ Shunyuan Li
li767679@sina.com

¹ Department of Anesthesiology, Quanzhou First Hospital
Affiliated to Fujian Medical University, Quanzhou 362000,
Fujian, China

are of great significance for improving clinical efficacy and prognosis, and prolonging their survival time.

Dexmedetomidine is a highly selective α_2 -adrenergic receptor agonist with sedative, analgesic, anti-sympathetic, and stress-reducing effects [9, 10]. It has been widely used in clinic because it has no significant respiratory depression effect [11, 12]. It has been reported that dexmedetomidine can function as a general anesthetized adjunct and reduce the amount of anesthetic drugs, thus maintaining hemodynamic stability and reducing patients' stress response during surgery [13]. The application of dexmedetomidine in cardiovascular surgery can also reduce the degree of restlessness and the incidence of hypertension in elderly hypertensive patients [14]. The application of dexmedetomidine infusion during laparoscopic surgery improves the cognitive function of patients and reduces the incidence of early postoperative cognitive dysfunction [15]. More importantly, in a craniotomy for the treatment of ischemic brain injury, dexmedetomidine treatment effectively reduces the content of various inflammation-related factors in patients' serum, including tumor necrosis factor (TNF)- α , interleukin (IL)-6, S100 calcium-binding protein- β (S100- β), superoxide dismutase (SOD) and cortisol [16]. Utilization of low-dose dexmedetomidine effectively accelerates the intestinal function recovery post-surgery [15]; however, the relationship between the use of dexmedetomidine in intestinal surgery and the postoperative inflammatory response of patients remains unclear.

In this study, we mainly investigated the inhibitory effect of dexmedetomidine on the systemic inflammation caused by intestinal surgery, and demonstrated that preoperative intravenous injection of dexmedetomidine reduced the incidence of inflammation. We believe that our research provides a theoretical basis for the clinical application of dexmedetomidine and helps to improve the prognosis and life quality of patients with intestinal surgery.

2 Methods

2.1 Study Design

To investigate the correlation between the application of dexmedetomidine and the physiological outcomes of patients with intestinal surgery, a randomized, controlled, and single-blinded clinical trial was performed in this study. We evaluated the anti-inflammatory effects of dexmedetomidine on patients undergoing intestinal surgery from 2019 to 2020, and aimed to recruit patients arranged for intestinal surgeries. Patients who participated in our

clinical trial were from Quanzhou First Hospital Affiliated to Fujian Medical University. This study was approved by the Ethics Committee of Quanzhou First Hospital Affiliated to Fujian Medical University (QZDIYY/2019/28), and followed the Declaration of Helsinki ethical principles for medical research involving human subjects.

2.2 Participants

Patients who met the following criteria were recruited in this clinical trial: (1) over 18 years of age; (2) meeting the American Society of Anesthesiologists (ASA) score I–II; (3) diagnosed by computed tomography (CT) and indicated for surgery; (4) no history of sedation and analgesics; (5) no contraindications for gastrointestinal surgery; (6) no dexmedetomidine allergies; and (7) signed informed consent and participated voluntarily. However, patients with the following situations were excluded from the trial: (1) combined respiratory and metabolic diseases; (2) combined endocrine and immune diseases; (3) stomach, liver and kidney dysfunction before surgery; (4) large-scale use of sedative drugs for a long period of time; (5) mental illness; and (6) disagree or were unwilling to cooperate with the investigator. The study was approved by the Ethics Committee of Quanzhou First Hospital Affiliated to Fujian Medical University.

A total of 86 patients meeting the above criteria were recruited and assessed for our study. Participants were randomly divided into two groups (dexmedetomidine group and control group) at a ratio of 1:1. Random allocation sequence was generated by a colleague who did not participate in this research. Among all patients, six participants were excluded due to multiple reasons such as allergy and drug use history; data were collected from the remaining 80 participants. Patients in the control group received an intravenous infusion of 0.9% saline 10 min before the induction of anesthesia, while participants in the dexmedetomidine group received an intravenous infusion of dexmedetomidine 10 min before the induction of anesthesia.

2.3 Interventions

A standardized anesthesia management protocol was applied among the groups. All patients were fasted for 12 h and deprived of water for 3 h. After entering the operating room, patients were connected to an automated system (IntelliVue MP50, Philips, Amsterdam, The Netherlands). Electrocardiogram (ECG), pulse oxygen saturation (SpO_2), heart rate (HR), blood pressure (BP), and bispectral index (BIS; Aspect A-2000, Aspect Medical Systems Inc., Newton, MA, USA) were routinely monitored.

Routine preoperative injection Diazepam (10 mg) and atropine (0.5 mg) were injected through the right internal jugular vein in hydroxyethyl starch 200/0.5 and sodium chloride injection at a rate of 6–8 ml kg⁻¹ h⁻¹. In the meantime, a left radial artery puncture was performed to monitor the invasive arterial pressure. Ten minutes before the induction of anesthesia, a loading dose of dexmedetomidine 1 µg/kg was injected by intravenous pump to the intervention group. Intravenous infusion of dexmedetomidine was then kept at a rate of 0.4 µg kg⁻¹ h⁻¹ until the end of operation. The same dose of saline was applied to the control group.

Anesthesia induction Midazolam 0.05 mg/kg, medium/long chain propofol 1.0–2.0 mg/kg, cisatracurium 0.10–0.15 mg/kg, and sufentanil citrate 0.3–0.4 µg/kg were injected intravenously. Patients were given mechanical ventilation with inhalation oxygen concentration of 60%, tidal volume of 6–8 mL/kg, ventilation frequency of 10 times/min, inspiratory/expiratory ratio of 1:2, and oxygen flow rate of 2.2 L/min. PetCO₂ was maintained at 35–40 mmHg (1 mmHg = 0.133 kPa).

Intraoperative maintenance Remifentanyl 0.1–0.2 µg kg⁻¹ min⁻¹ and propofol 3–5 mg kg⁻¹ H⁻¹ were infused intravenously and muscle relaxants were administered intermittently. During the operation, hemodynamic stability was maintained by adjusting the pump rate of remifentanyl and propofol, and BIS values were maintained at 45–55. During the operation, lactate Ringer's liquid was used to supplement physiological requirement, and hydroxyethyl starch 200/0.5 sodium chloride was injected to supplement blood loss. During anesthesia, the dosage was adjusted according to the changes in HR, BP, and other indicators. Vital signs were closely monitored and kept stable.

Postoperative management After the operation, when patients had recovered completely, the tracheal tube was pulled out and patients were sent to the anesthesia recovery room for patient-controlled intravenous analgesia. The analgesic solution formula dezocine 25 mg and tropisetron hydrochloride 10 mg was diluted to 100 mL with 0.9% normal saline for injection. The loading dose was 5 mL, background dose was 2 mL/h, additional dose was 1 mL/time, locking time was 10 min, and analgesia time was 48 h.

2.4 Data Collection

Two millimeters of blood was collected from the left radial artery of patients before administration (T0), 10 min after pumping dexmedetomidine/saline solution (T1), immediately after the operation started (T2), 30 min after the operation started (T3), and immediately after the operation ended (T4). The serum was separate by centrifugation and store at -20 °C

for further experiment. Enzyme-linked immunosorbent assay (ELISA) kits (R&D Systems, Minneapolis, MN, USA) were used to evaluate the circulating cytokines and proteins, including IL-6, TNFα, IL-8, and IL-10, while turbidimetry assay was used to evaluate the C-reactive protein (CRP) levels. The recovery time of spontaneous breathing, the time of tracheal tube removal, and the occurrence of postoperative agitation in the two groups of patients were recorded immediately after the operation. Mini-Mental State Examination (MMSE) was used to demonstrate the cognitive function of patients in each group before administration and 2, 6, 12 and 24 h after operation [17]. An MMSE score lower than 27 was considered as the incidence of postoperative cognitive dysfunction.

2.5 Statistical Analysis

To detect a difference of ≥ 20% in the cumulative number of inflammatory factors after operation, a sample size of 39 per group was required to have a study power of 80% ($\alpha = 0.05$, $\beta = 0.2$), i.e. a total of 78 patients. Assuming a dropout rate of 10%, a total of 86 patients were initially recruited for adequate data collection.

All data were obtained from three independently repeated measurements. The categorized variables are shown as frequency or percentage, while mean and standard deviation are utilized to demonstrate the continuous variables, all of which followed normal distribution. The Chi-square test (or Fisher's exact test) was used to compare the classification variables. One-way analysis of variance (ANOVA) and Tukey's post hoc test were used to analyze the continuous variables and a contingency table Chi-square test was acquired for the comparison of outcomes among different groups. SAS statistical software version 17.0 (SAS Institute Inc., Cary, NC, USA) was purchased for the statistical analysis in this study.

3 Results

3.1 Study Procedure

As shown in Fig. 1, a total of 86 patients meeting the above criteria were recruited and assessed for our study. Participants were randomly divided into two groups (dexmedetomidine group and control group). Participants in the dexmedetomidine group received intravenous dexmedetomidine 10 min before the induction of anesthesia.

3.2 Basic Characteristics of the Participants

The basic clinical characteristics of all participants were collected and are shown in Table 1. The demographic parameters collected from patients in the two groups included age,

sex, body mass index (BMI), basic diseases, preoperative indicators, and duration of surgery and anesthesia. As shown in Table 1, there were no significant differences in any of the above characteristics between participants in these two groups at the beginning of our research ($p > 0.05$).

3.3 Dexmedetomidine Treatment Suppressed Interleukin (IL)-6, IL-8, IL-10, Tumor Necrosis Factor- α and C-Reactive Protein Levels in Patients with Intestinal Surgery

Inflammation-related factors of patients at different time points in these two groups are shown in Fig. 2. ELISA assay was used to evaluate the serum cytokines, including IL-6 (Fig. 2a), IL-8 (Fig. 2b), IL-10 (Fig. 2c), and TNF α (Fig. 2d) at T0–T4. Compared with the control group, IL-6 levels were lower at T2–T4, IL-8 levels were lower at T3–T4, IL-10 levels were higher at T2–T4, and TNF α was lower at T2–T4 ($p < 0.05$). These differences suggested that dexmedetomidine infusion before anesthesia inhibited the systemic inflammation induced by intestinal surgery. The circulating CRP level of each patient was estimated by turbidimetry assay. Compared with the control group, the CRP levels of patients in the dexmedetomidine group were significantly lower at T2–T4 ($p < 0.05$) [Fig. 2e]. Therefore, treatment with dexmedetomidine before anesthesia significantly inhibited systemic inflammation during and post intestinal surgery.

3.4 Dexmedetomidine Treatment Reduced the Respiratory Recovery Time, Extubating Time, and Postoperative Agitation in Patients with Intestinal Surgery

The recovery time of patients' spontaneous breathing, time of tracheal tube removal, and occurrence of postoperative agitation of participants were recorded and are shown in Table 2. Furthermore, there were statistical differences between the respiratory recovery time ($p = 0.026$), extubation time ($p = 0.043$), and postoperative agitation ($p = 0.009$). Therefore, intravenous infusion of dexmedetomidine 10 min before anesthesia induction could not only improve the anesthesia effect but also promote the recovery of patients after anesthesia.

3.5 Dexmedetomidine Treatment Increased the Mini-Mental State Examination in Patients Post Intestinal Surgery

The MMSE was performed before administration and 2, 6, 12, and 24 h after surgery. As shown in Table 3, the MMSE scores of the dexmedetomidine group increased significantly at 2 h ($p = 0.032$), 6 h ($p = 0.008$), 12 h ($p = 0.029$), and 24 h ($p = 0.018$) post-surgery compared with the control group. Therefore, intravenous infusion of dexmedetomidine 10 min before anesthesia induction

Fig. 1 Flow diagram of the study. *DEX* dexmedetomidine

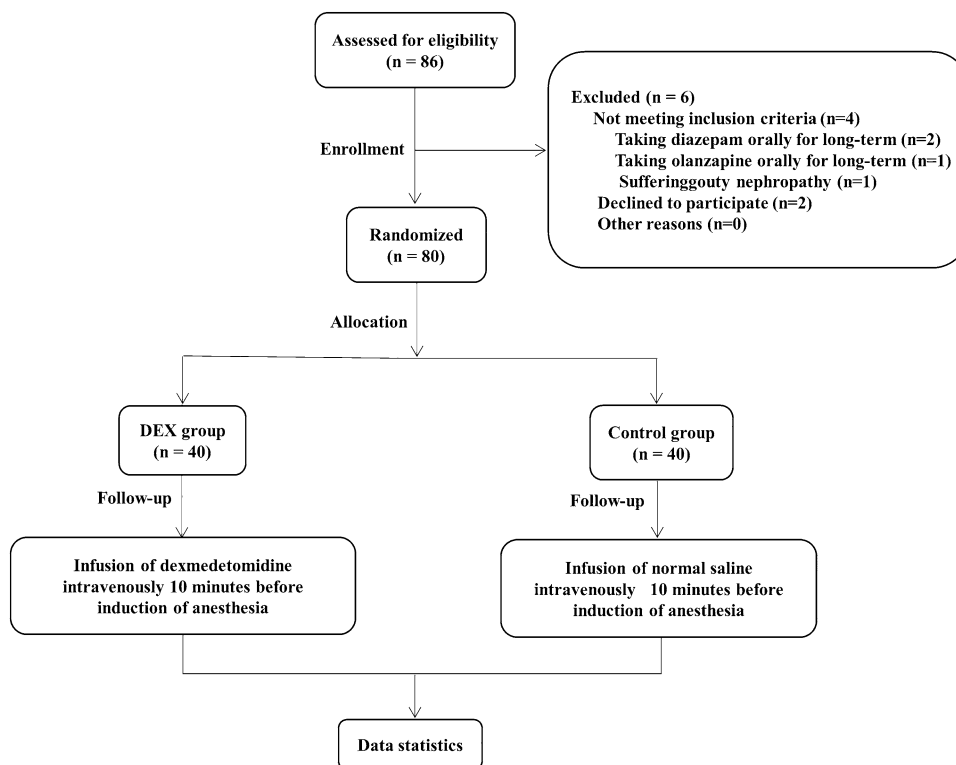


Table 1 Comparison of the two groups of patients using basic information

Items/groups	DEX group [n = 40]	Control group [n = 40]	p value
Age, years	50.76 ± 8.32	51.07 ± 9.43	0.816
Sex [n (%)]			0.329
Male	23 (57.5)	21 (52.5)	
Female	17 (42.5)	19 (47.5)	
Body mass index, kg/m ²	26.69 ± 5.08	26.87 ± 5.36	
Coexisting diseases [n (%)]			0.403
Hypertension	7 (17.5)	9 (22.5)	
Diabetes	5 (12.5)	6 (15.0)	
Dyslipidemia	13 (32.5)	15 (37.5)	
Preoperative indicators			
Heart rate, number/min	76 ± 11	77 ± 9	0.678
WBC counts, 10 ⁹ /L	6.23 ± 1.45	6.51 ± 1.19	0.314
Neutrophils, 10 ⁹ /L	9.03 ± 2.35	9.09 ± 2.44	0.509
Platelet count, 10 ⁹ /L	250.17 ± 44.86	244.87 ± 51.67	0.215
SpO ₂ , %	96.43 ± 5.16	96.18 ± 6.07	0.623
Duration of surgery, min	207.5 ± 19.4	214.4 ± 24.7	0.136
Duration of anesthesia, min	260.8 ± 26.3	265.2 ± 30.5	0.350

Data are expressed as mean ± SD

Participants in the DEX group received intravenous DEX 10 min before the induction of anesthesia

WBC white blood cell, SpO₂ pulse oxygen saturation, DEX dexmedetomidine, SD standard deviation

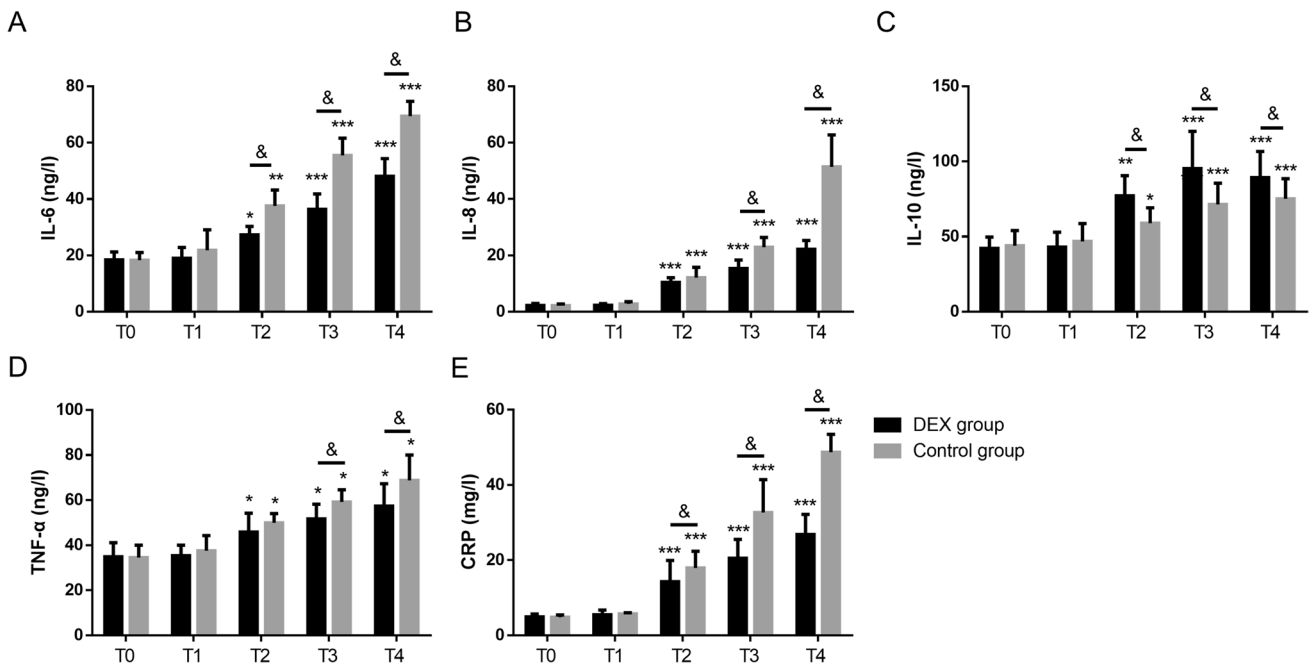


Fig. 2 Effect of dexmedetomidine administration on inflammation in patients undergoing intestinal surgery. Comparison of the value of **a** IL-6, **b** IL-8, **c** IL-10, **d** TNFα, and **e** CRP between the two groups of patients. Data are expressed as mean ± SD. **p* < 0.05, ***p* < 0.01,

and ****p* < 0.001 compared with T0. Data in bold indicate significant differences between the two groups. *IL* interleukin, *TNF* tumor necrosis factor, *CRP* C-reactive protein, *SD* standard deviation, *DEX* dexmedetomidine

Table 2 Comparison of the value of respiratory recovery time, extubation time, postoperative agitation, and remifentanyl consumption between the two groups of patients

Items/groups	DEX group [n = 40]	Control group [n = 40]	p value
Respiratory recovery time, min	6.54 ± 2.06	13.57 ± 4.36	0.026
Extubation time, min	13.48 ± 4.78	19.71 ± 3.82	0.043
Postoperative agitation, %	10	50	0.009
Consumption of remifentanyl intraoperatively, µg	343.7 ± 78.3	475.6 ± 79.2	0.002

Data in bold indicate the significant differences between the two groups

DEX dexmedetomidine

^aCompared with the control group, $p < 0.05$

Table 3 Comparison of the value of MMSE between the two groups of patients

Index	Timepoints	DEX group [n = 40]	Control group [n = 40]	p value
MMSE	T0	27.53 ± 6.45	27.79 ± 5.16	0.445
	2 h	24.15 ± 7.53***	23.35 ± 7.43***	0.032
	6 h	25.36 ± 4.62**	23.89 ± 6.14***	0.008
	12 h	26.93 ± 5.72*	24.76 ± 6.34**	0.029
	24 h	27.47 ± 5.35	26.09 ± 7.75*	0.018

MMSE Mini-Mental State Examination, SD standard deviation, DEX dexmedetomidine

Data are expressed as mean ± SD

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ compared with T0

The p -value indicates the significant differences between the two groups; data in bold indicate the significant differences between the two groups

effectively promoted the recovery of patients' postoperative cognitive ability.

3.6 Dexmedetomidine Treatment Reduced the Adverse Reactions in Patients Post Intestinal Surgery

Comparison of the incident of adverse reactions, including postoperative nausea and vomiting (PONV), shiver, respiratory depression, dizziness, and bradycardia, between the two groups of patients is shown in Table 4. Dexmedetomidine administration significantly decreased the incidence of PONV ($p = 0.008$), shiver ($p = 0.011$), and dizziness ($p = 0.013$), suggesting that intravenous infusion of dexmedetomidine could effectively reduce the adverse reactions caused by anesthesia.

4 Discussion

Generally, multiple factors, including anesthesia, intraoperative bed rest, surgery, and carbon dioxide stimulation, can affect patients undergoing intestinal surgery, resulting in weakening or even disappearing of gastrointestinal motility and increasing difficulty in the recovery of gastrointestinal function [18]. The surgery will not only cause the patient to lose a large amount of fluid in the intestinal cavity but also

Table 4 Comparison of the incident of adverse reactions between the two groups of patients

Index	DEX group [n = 40]	Control group [n = 40]	p value
Adverse reactions			
PONV	1 (2.5)	6 (15)	0.008
Shiver	2 (5)	12 (30)	0.011
Respiratory Depression	0 (0)	4 (10)	NA
Dizziness	3 (7.5)	10 (25)	0.013
Bradycardia	0 (0)	5 (12.5)	NA

Data are expressed as n (%)

Data in bold indicate the significant differences between the two groups

PONV postoperative nausea and vomiting, DEX dexmedetomidine, NA not available

increase the patient's intestinal and intra-abdominal pressure, resulting in clinical symptoms such as abdominal pain, bloating, and intestinal paralysis, which affects the treatment effect [19, 20]. Abdominal infection is one of the most common intraoperative and postoperative complications [21]. The main reasons include improper aseptic operation during the operation, damaged organs, and perforation or anastomotic rupture [22], which are also significant reasons why intestinal surgery can easily cause inflammation. In addition, during cardiopulmonary bypass (CPB) surgery, various

stimulating factors often cause a strong stress response in the human body, among which stress inflammatory response is very common in patients undergoing laparotomy and thoracotomy. The severe inflammatory reaction caused by intestinal surgery may lead to cell degeneration, necrosis, or abnormal metabolic function in the wound area [23]. Mechanical obstruction and compression caused by a large number of inflammatory exudates can seriously interfere with wound healing after surgery [24, 25]. In addition, the inflammation induced by surgery may lead to fever and changes in circulating immune cells, and eventually lead to different degrees of degeneration, necrosis, and dysfunction of the parenchymal cells of the heart, liver, kidney, and other organs [26]. Therefore, inhibiting the inflammatory response and reducing the level of inflammatory response in patients after bowel surgery are of great significance to improve the clinical efficacy and prognosis of patients. Furthermore, it is also of great significance for prolonging the survival time of patients undergoing intestinal surgery.

In this study, we mainly investigated the relationship between the application of dexmedetomidine and the outcomes of intestinal surgery patients. We showed that dexmedetomidine could effectively reduce the level of inflammatory factors circulating in patients during surgery and inhibit the inflammation caused by surgery. In addition, we also demonstrated that intravenous infusion of dexmedetomidine before anesthesia could improve the anesthetic effect and reduce the adverse reactions caused by anesthetic drugs. At the same time, dexmedetomidine could also promote the recovery time and speed of consciousness recovery after intestinal surgery. We believed that our research provided a new theoretical basis for the application of dexmedetomidine in bowel surgery.

Dexmedetomidine is a highly selective adrenergic α_2 receptor (α_2 AR) agonist; its ratio of binding to α_2 AR and α_1 -adrenergic receptor (α_1 AR) is 1600:1 [27, 28]. The affinity of dexmedetomidine with α_2 AR is several times that of clonidine [29], and its efficacy is precise and dose-dependent. Dexmedetomidine has definite anti-anxiety, sedation, and analgesic effects. Previous studies have shown that patients treated with dexmedetomidine before surgery ended up with significantly higher sedation scores than the control group [30]. Another study showed that even if the dose of dexmedetomidine reached multiple times the recommended dose, the patient's pulse, blood oxygen saturation, and arterial blood carbon dioxide partial pressure was still maintained within the normal range under the condition of inhaled air [31]. Thus, dexmedetomidine is widely used as a preoperative medication and its effect can continue until the induction period. Dexmedetomidine can be used in conjunction with other inducing drugs to deepen the depth of anesthesia and weaken the cardiovascular response, thereby reducing irritation, severe response, and difficult intubation

operations, including double-lumen bronchial intubation, obstructive tube intubation, and in the chest cannula used in surgery [32]. In addition, dexmedetomidine has the effect of strengthening vagal tone and reducing sympathetic tone, which allows the application of dexmedetomidine to reduce HR and prevent surgery- and stress-induced hypertension [33]. Accumulating evidence has demonstrated that dexmedetomidine can stimulate central and peripheral receptors, reduce sympathetic nerve activity and plasma catecholamine concentration, and reduce perioperative stress response [10]. Its ability to reduce sympathetic tension and indirectly increase parasympathetic tension is of great importance to reduce the occurrence of inflammation, inhibit the release of inflammatory factors, reduce cell apoptosis, and reduce the occurrence of sepsis. Since the relationship between the use of dexmedetomidine in intestinal surgery and the postoperative inflammatory response of patients is still unclear, our research may provide a new perspective on the clinical application of dexmedetomidine.

However, there were still some shortcomings in our research. Due to the limitation of resources and time, only 86 patients were included in this study and the small number of participants may have affected the accuracy of the results. In addition, since many patients experience multiple chronic diseases, the surgical medication and anesthesia scheme are different, which may affect the accuracy of our data. Some subjective factors might impact the research results. In this study, we mainly explored the inhibitory effect of dexmedetomidine treatment on anesthesia-induced systemic inflammatory response before anesthesia induction. The time we took the blood sample was also during and shortly after the operation. Therefore, the regulatory effect of dexmedetomidine on inflammation in the postoperative recovery of patients undergoing intestinal surgery is still not fully understood. Furthermore, in this experiment, we only adopted a single intravenous infusion method and dosage. Different administration methods and dosages are likely to affect the effect of dexmedetomidine on the inflammatory response of patients. Therefore, in the following research, we will continue to pay attention to these problems and try to design some new experiments to solve these deficiencies in this research.

5 Conclusion

We mainly investigated the relationship between the application of dexmedetomidine during the intraoperative period and the outcomes of intestinal surgery patients in this research. We demonstrated that dexmedetomidine could effectively reduce the level of serum inflammatory factors in patients and inhibit the inflammation caused by intestinal

surgery. Dexmedetomidine also alleviated the patient's stress response and promoted the recovery of the patient's cognitive ability. We believe that our research can provide a theoretical basis for the clinical application of dexmedetomidine and help to improve the prognosis and life quality of patients undergoing intestinal surgery. Nevertheless, this study was more focused on inflammation and the relative events. It is of great interest to also explore, in future studies, the effect of dexmedetomidine on gastrointestinal function recovery in patients undergoing intestinal surgery.

Declarations

Funding This study was supported by Quanzhou Science and Technology Project (2019N042S).

Conflict of interest Rushuang Chen, Zhenming Kang, Yaduan Wang, Jie Zhao, and Shunyu Li declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics approval This study was approved by the Ethical Committee of Quanzhou First Hospital Affiliated to Fujian Medical University.

Consent to participate Written informed consent for publication of this paper was obtained from the Quanzhou First Hospital Affiliated to Fujian Medical University.

Consent for publication Written informed consent was obtained from patients for the publication of this study and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and material Data will be made available upon reasonable request.

Code availability Not applicable.

Author contributions RC, ZK, YW, JZ, SL conducted the experiments, collected and analyzed the data, and wrote the manuscript. SL conceived and supervised the study.

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