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Review Article

Effect of dexmedetomidine on hemodynamics and stress response of laparoscopic surgery in children

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Abstract: This study intended to investigate the role of dexmedetomidine on hemodynamics and stress response of laparoscopic surgery in children. The pain and agitation of the two groups of children were evaluated, and the minimum alveolar concentrations (MAC) of the two groups of children were evaluated. The changes of postoperative blood oxygen saturation (SpO2), mean arterial pressure (MAP), heart rate (HR), and concentrations of serum cortisol and epinephrine were evaluated. In addition, the recovery room dwell time and wake time of the two groups and the occurrence of adverse reactions after treatment were explored. The VAS score of the research group (RG) was significantly lower than that of the control group (CG) after therapy (P<0.05), and the sedation-agitation scale (SAS) score and MAC value of RG were lower than those of CG after operation (P<0.05). MAP and HR at T1, T2 and T3 in RG were lower than those in CG (P<0.05). The concentrations of cortisol and epinephrine in RG were lower than those in CG at T1, T2 and T3, P<0.05. The recovery room dwell time and recovery time in RG were shorter than those in CG, P<0.05. The adverse reactions in RG were significantly less than those in CG (P<0.05). Dexmedetomidine can take a good analgesic and sedative effects in pediatric laparoscopic surgery and can reduce stress response and stabilize hemodynamics, so it is worthy of popularization and application in pediatric laparoscopic surgery in the future.

Keywords: Dexmedetomidine, laparoscopic surgery in children, hemodynamics, stress response

Introduction

Laparoscopic surgery (LS) is a newly developed minimally invasive therapy, which is inevitable in the development of surgical methods [1]. With the rapid development of industrial manufacture technology, the integration of relevant disciplines has laid a firm foundation for the development of new technologies and methods [2]. Combined with the increasingly skilled operation of doctors, many previous open surgeries have been replaced by endovascular surgeries, which greatly increase the selection of surgical methods [3]. In laparoscopic surgery, several small incisions with a diameter of 5-12 mm are made in different parts of the abdomen, the camera lens and various special surgical instruments are inserted through these small incisions, and the surgeons complete the operation by observing the images and using various surgical instruments in vitro [4, 5]. The advantages of laparoscopic surgery are very obvious, including small trauma, short hospital stay, and quick recovery, which greatly reduce the burden and cost of patients [6]. Currently, LS has been widely used in clinical practice, especially in some minor pediatric surgeries such as appendicitis and inguinal hernia [7]. However, due to the younger age and surgical stress, anesthesia is required for children during surgery.

Sevoflurane is a commonly used anesthetic drug for laparoscopic surgery [8] in children and has a low blood-gas partition coefficient, which is easy for anesthesia regulation and is not prone to stimulating the respiratory tract, so the children can wake up quickly after surgery [9]. However, recent studies have shown that sevoflurane has a strong adverse effect on chil-

dren's postoperative recovery. Shi et al. have shown that sevoflurane is a crucial factor leading to dysphoria in children's recovery period, with high occurrence rate, which seriously affects children's postoperative recovery [10]. Dexmedetomidine is a highly selective α2 adrenoceptor agonist. It mainly acts below the cerebral cortex and acts on the cerebral locus coeruleus receptor to exert sedative and hypnotic effects similar to normal sleep [11]. Previous studies have shown that dexmedetomidine has a good sedative effect in laparoscopic surgery for inguinal hernia in children [12]. In order to further determine the application value of this anesthesia method in clinical pediatric laparoscopy, this study investigated the influence of dexmedetomidine on hemodynamics and stress response of pediatric laparoscopy, with the goal of providing a reliable theoretical basis for future clinical application of this anesthesia method.

Data and methods

General data

A total of 116 children admitted to Huzhou Hospital of Chinese Medicine for laparoscopic surgery from May 2016 to May 2018 were enrolled as research participants, including 56 children who underwent inguinal hernia repair and 60 children who underwent appendectomy. Forty-nine of them were anesthetized with sevoflurane and selected as the control group (CG). Another 67 children received dexmedetomidine on the basis of the CG as the research group (RG). This study was approved by the Ethics Committee of Huzhou Hospital of Chinese Medicine and was performed in accordance with Helsinki Declaration. All the above participants signed informed consent forms.

Inclusion and exclusion criteria

Inclusion criteria: Children who could apply laparoscopic surgery according to appendicitis diagnosis and inguinal hernia diagnosis; children who were followed-up in our hospital after diagnosis; children with complete case data; and those who agreed to cooperate with the medical staff.

Exclusion criteria: Children with central or peripheral nervous system diseases, liver and kidney dysfunction, local anesthetic or other drug allergy; children who had received long-term analgesic and sedative drug therapy; children with coagulation dysfunction, multiple tumors, and physical disability, and those transferred from the other hospital.

Method

All children were forbidden to drink and fasted for 6 hours. Routine ECG monitoring was carried out to the children after they entered the operative room, and anesthetic parameters were set according to the physical condition of children. All the children were induced by sevoflurane. The oxygen flow rate was adjusted to 6 L/min and sevoflurane to 8%. After rapid inflation for several times, the air in the anesthesia circuit was discharged and the mask was tightened closely to enable the children to fully inhale sevoflurane. After eyelash reflex disappeared, the oxygen flow rate and sevoflurane concentration were reduced. The children were given 0.6 $mg \cdot kg^{-1}$ of rocuronium bromide injection and 0.4 $\mu g \cdot kg^{-1}$ of sufentanil citrate injection. The children were intravenously injected and endotracheal intubation was performed. During the operation, sevoflurane concentration was maintained at 4-5%, remifentanil was injected at 0.5-1 $\mu g \cdot kg^{-1} \cdot min^{-1}$. The inhalation concentration of sevoflurane was adjusted according to the vital signs of children. Ten minutes before the end of the operation, the research group were given continuous intravenous infusion of 0.5 $\mu g \cdot kg^{-1}$ of dexmedetomidine, generally for 10 min. At the end of the operation, remifentanil and sevoflurane were stopped, and the oxygen flow was adjusted to 4 $L \cdot min^{-1}$. After the vital signs were stabilized, the children were sent to the anesthesia recovery room.

Outcome measures

Primary outcome measures: Pain degree: The visual analog scale (VAS) was adopted to assess the pain degree of children in the two groups [13]. Agitation: The sedation-agitation scale (SAS) was adopted to assess the agitation of patients in the two groups [14]. Hemodynamics: The minimum alveolar concentration (MAC) of children in the two groups was evaluated using the Dixonin. The postoperative blood oxygen saturation (SpO2), mean arterial

Table 1. General data comparison [n (%)]

Factor	Research group (n=67)	Control group (n=49)	X^2/t	P
Age	6.8±3.1	7.3±2.6	0.917	0.361
BMI (KG)	19.31±3.94	18.43±3.76	1.211	0.228
Gender			0.030	0.863
Male	38 (56.72)	27 (55.10)		
Female	29 (43.28)	22 (44.90)		
Residence			0.304	0.581
Urban	56 (83.58)	39 (79.59)		
Rural	11 (16.42)	10 (20.41)		
Nationality			0.808	0.369
Han	61 (91.04)	42 (85.71)		
Minorities	6 (8.96)	7 (14.29)		
Mode of delivery			0.433	0.511
Natural birth	41 (61.19)	27 (55.10)		
C-section	26 (38.81)	22 (44.90)		
Family history			0.022	0.881
Yes	21 (31.34)	61 (32.65)		
No	46 (68.66)	61 (67.35)		
One-child			0.998	0.318
Yes	52 (77.61)	34 (69.39)		
No	15 (22.39)	15 (30.61)		

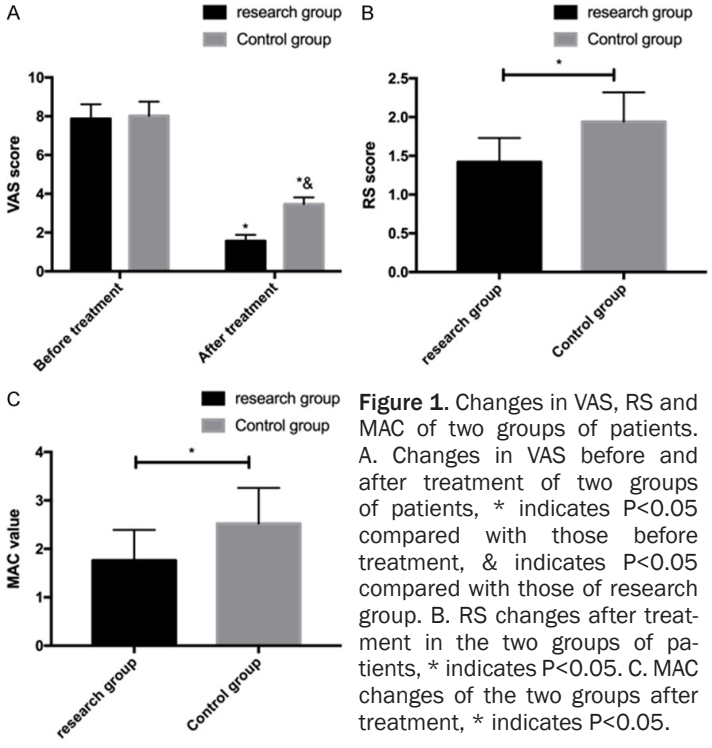

Figure 1. Changes in VAS, RS and MAC of two groups of patients. A. Changes in VAS before and after treatment of two groups of patients, * indicates P<0.05 compared with those before treatment, & indicates P<0.05 compared with those of research group. B. RS changes after treatment in the two groups of patients, * indicates P<0.05. C. MAC changes of the two groups after treatment, * indicates P<0.05.

pressure (MAP), and heart rate (HR) of them were also evaluated. Stress response: The concentrations of serum cortisol and epinephrine were determined using the enzyme-linked immunosorbent assay (ELISA).

Secondary outcome measures: Recovery: The recovery room dwell time and wake time of children in the two groups were evaluated. Adverse reactions: The occurrence of adverse reactions after operation in the two groups was explored.

Statistical method

The results were processed by SPSS24.0 (Shanghai Yuchuang Network Technology Co., Ltd). Counting data were expressed as rate, and chi-square test was applied for group comparison. The measurement data were expressed as mean ± SD. T test was applied for inter-group comparison, and one-way analysis of variance and LSD back testing for the multi-group comparison. P<0.05 indicates a significant difference.

Result

General data comparison

Comparing the general data of the two groups, it was found that there was no significant difference in age, BMI, sex, residence, nationality, mode of delivery, family history and one-child situation (all *P*> 0.05). See **Table 1**.

Changes of VAS, SAS and MAC in two groups of patients

The changes of VAS, SAS and MAC were evaluated, and it was revealed that the VAS score of CG and RG had no statistical difference before operation (P>0.05). The VAS score of RG was significantly lower than that of CG after treatment (P<0.05), and the SAS score and MAC value of the RG after treatment were all lower than those of CG (P<0.05). See **Figure 1**.

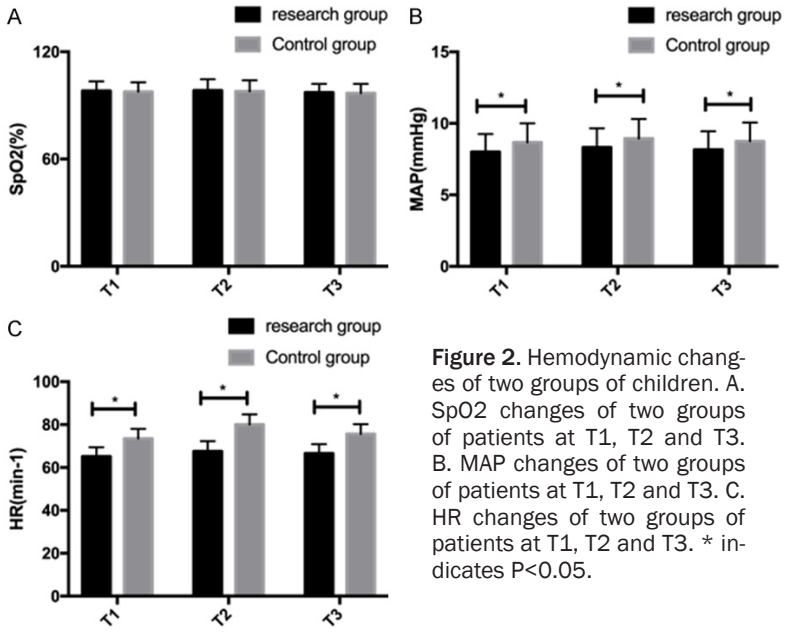

Figure 2. Hemodynamic changes of two groups of children. A. SpO2 changes of two groups of patients at T1, T2 and T3. B. MAP changes of two groups of patients at T1, T2 and T3. C. HR changes of two groups of patients at T1, T2 and T3. * indicates P<0.05.

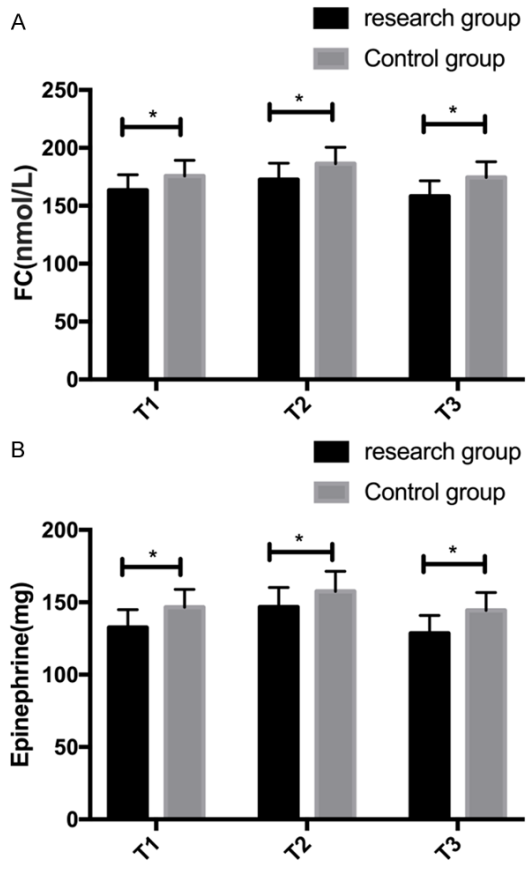

Figure 3. Stress response of two groups of children. A. Changes in serum cortisol of two groups of patients at T1, T2 and T3. B. Changes in epinephrine of two groups of patients at T1, T2 and T3. * indicates P<0.05.

Changes of hemodynamics in two groups

The changes of SpO2, MAP, and HR before operation (T1), immediately after extubation (T2), and 10 min after extubation (T3) were evaluated, and it was revealed that there was no significant difference in SpO2 between CG and RG at T1, T2 and T3 (P>0.05). The MAP and HR of RG at T1, T2 and T3 were lower than those of CG (P<0.05). See **Figure 2**.

Stress reaction of two groups of children

Arterial blood (2 mL) was sampled from each child in the two groups at T1, T2, and T3, and the concentrations of serum cortisol and epinephrine in the blood were determined. The results revealed that the concentrations of serum cortisol and epinephrine in RG were lower than those in CG at T1, T2 and T3 (P<0.05). See **Figure 3**.

Recovery room dwell time and wake time of two groups

The recovery room dwell time and wake time of RG and CG were evaluated and it was found that recovery room dwell time and wake time of RG were shorter than those of CG (P<0.05). See **Figure 4**.

Incidence of post-therapy adverse reactions in two groups

The incidence of postoperative adverse reactions in the two groups of children was evaluated. It was revealed that the incidence of adverse reactions in RG was 3 (4.48) and that in CG was 12 (24.49), and the difference was statistically significant (P<0.05). See **Table 2**.

Discussion

Laparoscopy does not require large-scale section, and compared with traditional surgery, the operation has small trauma and high safety,

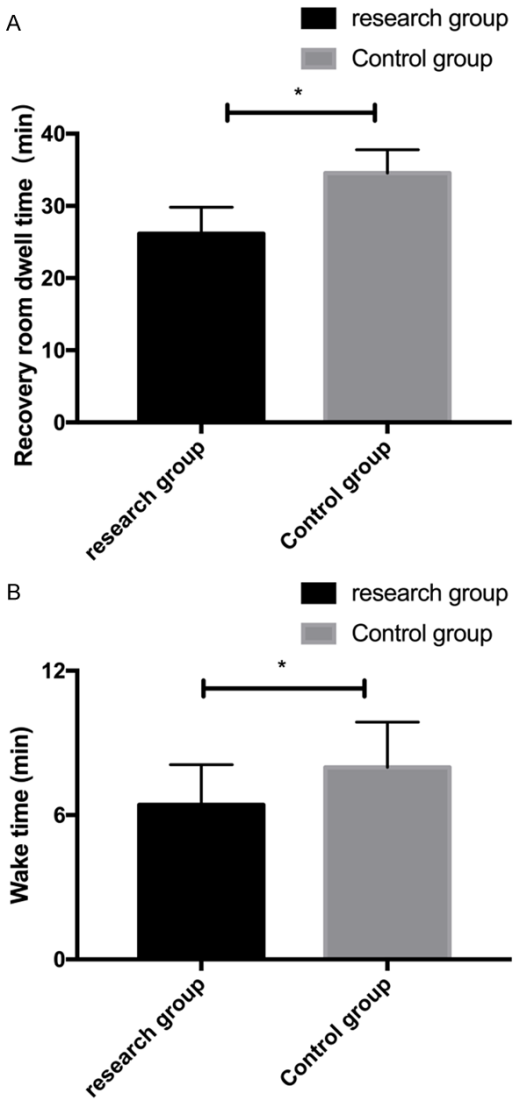

Figure 4. Recovery room dwell time and wake time of two groups of children. A. Comparison of recovery room dwell time of two groups of children. B. Comparison of wake time of two groups of children. * indicates $P<0.05$.

which is more suitable for pediatric surgery [15]. Due to the limited tolerance of children, anesthetic drugs should be carefully selected in laparoscopic surgery [16]. Adverse reactions such as stress reaction and increase of metabolic rate will greatly reduce the treatment efficiency and postoperative recovery due to the pain of children [17]. Therefore, appropriate analgesia and sedation are required during and after the operation to relieve or inhibit pain stress reaction, and reduce side effects caused by stress, so as to improve the therapeutic effect of children and reduce harms caused by stress reaction to children. Therefore, this experiment explored the effect of dexmedetomidine on pediatric laparoscopic hemodynamics and stress response. The results are as follows:

This study showed that the postoperative pain score of RG was significantly lower than that of CG, and the SAS score and MAC value were both lower than those of CG, which suggested that the application of dexmedetomidine had better sedation effect than sevoflurane for children's analgesia, and effectively controlled the MAC value change after sevoflurane inhalation anesthesia. SAS score is the postoperative restlessness score. Younger children are prone to awakening restlessness after surgical treatment, which is a mental state of behavior and consciousness separation, with symptoms such as disorientation, dysphoria and excitement. Although restlessness is self-limiting, it is also easy to induce many adverse events such as catheter extraction, wound bleeding, and dehiscence, which increases the pain of children and affects the therapeutic effect [18]. MAC mainly refers to an alveolar concentration of anesthetic when body motion reaction occurs under slice stimulation, and is an effective indicator for evaluating the efficacy intensity of inhalation anesthesia [19]. Dexmedetomidine is a highly selective α2 receptor agonist. It inhibits nerve impulse transmission by regulating hyperpolarization of locus coeruleus and nucleus pulposus and reducing NE release. At the same time, dexmedetomidine also has significant inhibitory effect on nociceptive stimulation transmission of spinal dorsal horn neurons, thus exerting certain analgesic and anxiolytic effects, reducing stress response of patients to pain stimulation, and relieving adverse emotional experience caused by pain [20]. Lundorf et al. have shown in their research that dexmedetomidine has a better effect in the treatment of acute pain after abdominal surgery in adults during perioperative period [21]. This further proved our experimental results. In order to further determine the analgesic and sedative effects of dexmedetomidine, we also evaluated the hemodynamic changes and stress responses of children in the two groups, and found that before operation, immediately after extubation, and at 10 min after extubation, the MAP and HR of the

Table 2. Incidence of post-therapy adverse reactions in two groups of children

	Research group n=67	Control group n=49	X^2	p
Anxiety and crying	2 (2.90)	9 (18.37)		
Laryngospasm	0 (0.00)	1 (2.04)		
Increased respiratory secretions	1 (1.49)	2 (4.08)		
Total incidence%	3 (4.48)	12 (24.49)	10.070	0.002

research group were significantly lower than those of the control group, and the concentrations of serum cortisol and epinephrine of the research group were also lower than those of the control group. MAP is the mean arterial pressure in a cardiac cycle [22]. HR, also named quiet HR, is the number of beats per minute of people in a quiet state, with generally 60-100 beats/minutes, and individual differences may occur due to age, sex, and other physiological factors [23]. From the analysis of hemodynamic results, we speculated that dexmedetomidine can directly act on α2 adrenergic receptors in spinal cord and brain, inhibit the discharge of central neurons, further exert analgesic, sedative and anxiolytic effects, and ensure the stability of respiratory circulation, thus stabilizing hemodynamics. Singla et al. mentioned that dexmedetomidine could reduce blood pressure in laparoscopic surgery [24], which was similar to our research results. Serum cortisol is produced and secreted by adrenal cortex and belongs to steroid glucocorticoids, whose secretion is regulated by adrenocorticotropic hormone in anterior pituitary. The determination of serum cortisol directly reflects the secretory function of adrenal cortex [25]. Epinephrine is a hormone secreted by the human body. When a person undergoes certain stimulation (including excitement, fear, and tension) and secretes this chemical substance, it can accelerate people's breathing, HR and blood flow, pupil enlargement, supplement more energy for body activities, and accelerate the reaction. Epinephrine is a hormone and neurotransmitter, which is released by the adrenal gland [26]. Stress reaction is a systemic nonspecific reaction after the body is strongly stimulated by internal and external environment. During stress, due to activation of hypothalamus-pituitary-adrenal cortex axis, the release of adrenocorticotropic hormone increases and cortisol enters blood in large quantities. Meanwhile, adverse stimulation leads to glycogen decomposition, increases gluconeogenesis and Glu concentration [27]. From the stress response of the two groups of children, we suspected that dexmedetomidine could reduce sympathetic nerve activity and the concentration of serum cortisol and epinephrine in children, thus inhibiting stress response. In addition, one study by Li et al. showed that dexmedetomidine could reduce stress response after gynecological laparoscopic surgery, further supporting our experimental results [28]. Finally, we recorded the recovery room dwell time, wake time and postoperative adverse reactions. The results revealed that those in RG were lower than CG. Therefore, this result further demonstrated that dexmedetomidine could effectively control postoperative pain, hemodynamics and stress reactions of the children, and further verified our above experiments. Therefore, we could conclude that dexmedetomidine has provided better analgesic and sedative effects, stabilized hemodynamics, and reduced stress response in pediatric laparoscopic surgery.

However, there are still deficiencies in this experiment. There are many anesthesia schemes used in surgery, but we have not compared the scheme in this study with other anesthesia schemes. Due to the short research time, we have not recorded the prognosis of children for a long time after surgery. There are many methods of anesthesia and analgesia in clinical practice, but we have not determined different effects on postoperative analgesia, hemodynamics and stress response of children after laparoscopic surgery by other analgesic methods. We will conduct better experiments and comprehensive analysis as soon as possible according to the above deficiencies to get better experimental results.

In conclusion, dexmedetomidine has good analgesic and sedative effects in pediatric laparoscopic surgery and can reduce stress response and stabilize hemodynamics, it is worthy of promotion and use in pediatric laparoscopic surgery in the future.

Disclosure of conflict of interest

None.

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