Clinical Observation of Intranasal Dexmedetomidine in Pediatric Patients Undergoing Laparoscopic High Ligation for Incarcerated Inguinal Hernia

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Abstract: Objective To observe the effect of Dexmedetomidine intranasal drop on induction compliance, emergence delirium and post hospitalization behavior change in children undergoing laparoscopic high ligation for incarcerated inguinal hernia.Methods Ninety children undergoing laparoscopic high ligation for incarcerated inguinal hernia were randomly divided into 3 groups: dexmedetomidine group 1 (Group D1), dexmedetomidine group 2 (Group D2), and control group (Group C),with 30 cases in each group. 30 minutes before anesthesia induction, Group D1 received dexmedetomidine intranasal drop 1 μg·kg-1, Group D2 received dexmedetomidine intranasal drop 2 μg·kg-1, Group C received normal saline. ICC score, PAED score, PHBQ case, MAP,HR,SpO2 and adverse reaction were recorded. Results Compared with T0 and group C,group D1,MAP and HR in group D2 decreased significantly (P<0.05).Compared with T0 and group C, group D1,SpO2 in group D2 there was no statistical significance (P>0.05). Compared with group C, ICC score, PAED score and PHBQ case in group D1 and D2 decreased significantly (P <0.05). Compared with group D1, ICC score, PAED score and PHBQ case in group D2 there was no statistical significance (P>0.05).No obvious adverse reaction observed in 3 groups. Conclusion Dexmedetomidine preoperative intranasal drop 1 μg·kg-1 in children undergoing laparoscopic high ligation for incarcerated inguinal hernia could increase anesthesia induction compliance, decrease emergence delirium and post hospitalization behavior change, with no obvious adverse reaction. Dexmedetomidine intranasal drop 2 μg·kg-1 provide the same effect in anesthesia induction compliance, emergence delirium and post hospitalization behavior change, but MAP and HR decreased significantly.

1. Introduction

Inguinal hernia is a common disease in pediatric surgery. Surgical treatment is the most effective treatment for inguinal hernia of pediatric patients.[1]Children's concerns relevant to surgery include fear of separation, perioperative period depression or behavioral abnormality, and fear of physical integrity. These concerns can be manifested as fear, dysphoria, urinary incontinence, and extreme strain before operation and during anesthesia induction period[2]. Crying, struggling and shouting before operation of pediatric patients may lead to respiratory secretion increase, flatulence of digestive tract and other anesthesia risks, as well as post hospital behavior change[3]. Dexmedetomidine (DEX) is a new highly selective α_2AR agonist, which incurs a relatively rapid effect by activating α_2AR of locus coeruleus. It is more difficult for pediatric patients to adopt open vein method for medication prior to surgery than for adults, and non-invasive drug administration is easier for pediatric patients to accept and implement. This study intends to investigate the effects of different doses of intranasal drop DEX for pediatric patients undergoing laparoscopic high ligation for incarcerated inguinal hernia, and observes the effects of anesthesia induction cooperative level, emergence delirium and post hospitalization behavior change on children patients.

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2. Materials and Methods

2.1 General Materials

With the approval of the Ethics Committee of Ningbo Women and Children's Hospital, 90 pediatric patients undergoing Laparoscopic High Ligation were selected for incarcerated inguinal hernia from April 2017 to October 2017. With Informed Consent Form signed before operation, the patients consists of 52 males and 38 females, ASA I-II, aged 1-5 years, 10-20 kg in weight. Exclude the pediatric patients who are allergic to any drug in the study, suffer nose disease, organ dysfunction, arrhythmia, cardiopulmonary disease, risk of airway obstruction, developmental retardation, or receive anticonvulsant treatment, as well as the patients whose guardian refused to join in. Divide into 3 groups by random number table method: group Dex1 (group D1), group Dex2 (group D2) and control group (group C), with 30 cases in each group.

2.2 Dex Intranasal Drop

The pediatric patient was escorted into the waiting area by one parent 30 minutes before anesthesia induction. Clean the nasal cavities carefully for patients with cotton swabs. Pump 1 ml intranasal drop solution into a syringe without needle, and drip by drops carefully into the bilateral nasal cavities of the patient, to prevent the outflow of drugs. After dropping, gently rub the bilateral alars several times. During intranasal drop, let the patient lie in the arm of the parent with the patient's head raised slightly. After 5 minutes after intranasal drop, the pediatric patient may select comfortable posture freely. HR and SpO_2 were measured before and after intranasal drop. Exclude the pediatric patient not cooperative and replace with eligible pediatric patient to join the group, to keep 30 children in each group. Apply Dex 1 $\mu g \cdot kg^{-1}$ for group D1, Dex 2 $\mu g \cdot kg^{-1}$ for group D2, and normal saline for group C. Dilute with normal saline for groups D1 and D2, to reach a total amount of 0.4 ml for the intranasal drop of the three groups.

2.3 Anesthesia Induction and Maintenance

After 30 minutes of intranasal drop, transport the pediatric patient to the operating room with transfer bed. Monitor ECG, NIBP, SpO_2 and $P_{ET}CO_2$ as a matter of routine. Provide 8% sevoflurane inhalation induction through mask. After the disappearance of eyelash reflexes, place laryngeal mask of the corresponding type. After correct placement, provide mechanical ventilation to adjust and maintain the respiratory parameters in the normal range for the pediatric patient. Adjust the concentration of sevoflurane and maintain at 1.3 Mac. Adjust the pediatric patient to the left lying position, confirm the position of laryngeal mask, observe the respiratory parameters closely, and carry out sacral puncture at the same time. After successful puncture, 0.8% pre-made lidocaine was injected into sacral canal by 1 ml / kg weight. Adjust the pediatric patient to supine position, confirm the position of laryngeal mask again, and start the operation. At the completion of the operation, gradually reduce the concentration of sevoflurane until cutting off completely. Confirm the spontaneous respiration and the restoration of swallowing and choking reflex of the pediatric patient. When the respiratory rate is >10 times / min, the tidal volume is >6 ml $\cdot$ kg^{-1}, and the oxygen saturation is > 95% (inhaling air), take off the laryngeal mask. After reaching stable vital signs, transfer to the anesthesia recovery room. After transferred to the anesthesia recovery room and one hour's observation by the anesthetist, transfer the pediatric patient to the ward after reaching the leaving standard. In case of any necessity for vasoactive drugs in the perioperative period, the pediatric patient should be treated accordingly and excluded from this study.

2.4 Observation Indexes

Record the HR, MAP and SpO_2 immediately before intranasal drop (T0), 10 minutes after intranasal drop (T1), 20 minutes after intranasal drop (T2), during anesthesia induction (T3), at the beginning of surgery (T4), and when taking off laryngeal mask (T5). Record the anesthesia time, operation time and adverse reactions (regurgitation aspiration, laryngospasm, bucking, labored breathing, vomiting, apnea, etc.). Score in induction compliance checklist (ICC) during anesthesia

induction. Adopt pediatric anesthesia emergence delirium(PAED) for pediatric patient emergence delirium when taking off the laryngeal mask. Train the parents during preoperative visits with the post hospitalization behavior questionnaire (PHBQ), to introduce the scoring standard of the scale in detail for evaluation and report by the parents one week after the operation.

2.5 Statistics Process

According to the normality test of measurement data carried out, the data complies with the normal distribution, so the average ± standard deviation is adopted for statistical description. Adopt one-way variance analysis for comparison between different groups at the same time point, and single-group repeated measurement variance analysis for comparison between different time points in the same group. In case of any difference with statistically significance, adopt LSD-t method for pairwise comparison. Adopt χ^2 test for comparison of classification data groups. All the statistical analysis was completed in SPSS 20.0, and the test level was $\alpha = 0.05$.

3. Results

1) Comparison of Patient Characteristics

The differences in age, weight and gender among the three groups of pediatric patients had no statistical significance (*P > 0.05*). See Table 1.

Table 1 Comparison of Patient Characteristics

Groups	Number of Cases	Age (Year)	Weight (kg)	Male/Female
Group C	30	2.9±0.9	14.3±2.7	19/11
Group D1	30	2.8±0.9	13.8±2.3	17/13
Group D2	30	3.3±1.1	14.9±2.4	16/14

2) Comparison of Anesthesia Time and Operation Time.

The differences in anesthesia duration and operation duration among the three groups of pediatric patients had no statistical significance (*P > 0.05*). See Table 2.

Table 2 Comparison of Anesthesia Time and Operation Time

Groups	Anesthesia Duration (min)	Operation Duration (min)
Group C	30.8±5.9	24.3±6.4
Group D1	27.4±6.7	23.7±5.8
Group D2	29.5±6.2	25.4±7.2

3) Comparison of Map, Hr, and Spo_2 in 3 Groups

MAP: There was no statistical difference between T1~T5 and T0 for group D1 and group C (*P > 0.05*); there was no statistical difference among T1, T3 and T0 for group D2 (*P > 0.05*), and MAP levels of T2, T4 and T5 were significantly lower than that of T0 (*P < 0.01*); compared with group C and group D1, MAP levels of T0, T1 and T3 in group D2 had no statistical difference (*P > 0.05*), and MAP levels of T2, T4 and T5 in group D2 were lower than those in group C and group D1 (*P < 0.05*). See Table 3.

HR: Compared with group C and group D1, there was no significant difference in MAPs of T0, T1 and T3 in group D2 (*P > 0.05*). HR levels of T2, T3, T4 and T5 were significantly lower than that of T0 (*P > 0.01*); Compared with group C and group D1, HR levels of T2, T3, T4 and T5 were significantly lower than those of group C and group D1 (*P < 0.01*). See Table 4.

SpO_2: For the three groups, there was no statistical difference between SpO_2 and T0 from T1 to T5 (*P > 0.05*); compared with group C and D1, there was no statistical difference among SpO_2s of T0, T1, T2, T3, T4 and T5 in group D2 (*P > 0.05*). See Table 5.

4) Comparison of Various Scores in 3 Groups

Compared with group C, the ICC scores and PAED scores of groups D1 and D2 were significantly lower than those of group C (*P < 0.01*); Compared with group D2, group D1 had no

significant statistical difference ($P > 0.05$); the PHBQ ratios of group D1 and group D2 were significantly lower than that of group C ($P < 0.05$), and there was no significant difference between PHBQ ratios of group D1 and group D2 ($P > 0.05$). See Table 6.

Table 3 Comparison of MAP(mmHg) in 3 Groups

Groups	T0	T1	T2	T3	T4	T5
Group C	78.8±10.2	77.0±6.9	76.9±9.2	74.2±8.1	78.1±6.5	80.7 ± 6.4
Group D1	78.2±4.8	78.0±4.3	76.6±7.6	76.2±7.1	79.2±6.8	78.8 ± 6.1
Group D2	78.4±7.3	79.8±4.4	71.2±8.5^{aabc}	78.5±5.6	71.6 ± 6.5a^{aabbcc}	72.5 ± 8.2^{aabbcc}

Note: For in-group comparison: compared with T0, $^{a}P<0.05$,$^{aa}P<0.01$; For comparison among groups: compared with group C, $^{b}P<0.05$,$^{bb}P<0.01$; compared with group D1, $^{c}P<0.05$, $^{cc}P<0.01$.

Table 4 Comparison of HR in 3 Groups

Groups	T0	T1	T2	T3	T4	T5
Group C	115.7±9.2	114.4±8.1	111.1±8.9	112.8±8.6	111.4±7.9	112.8±8.4
Group D1	113.7±9.6	113.7±9.9	109.5±10.9	110.6±9.0	110.6±9.8	114.1±9.5
Group D2	115.1±7.9	110.4±10.9	97.6 ± 10.7^{aabbcc}	93.3 ± 8.7^{aabbcc}	99.3 ± 8.4^{aabbcc}	102.3 ± 7.8^{aabbcc}

Note: For in-group comparison: compared with T0, $^{a}P<0.05$,$^{aa}P<0.01$; For comparison among groups: compared with group C, $^{b}P<0.05$,$^{bb}P<0.01$; compared with group D1, $^{c}P<0.05$, $^{cc}P<0.01$.

Table 5 Comparison of SpO2(%) in 3 Groups

Groups	T0	T1	T2	T3	T4	T5
Group C	98.6±1.10	98.9±1.09	99.0±1.00	98.7±1.05	98.5±0.97	98.9±0.99
Group D1	98.9±0.99	98.7±1.23	98.8±1.04	99.1±0.92	98.8±0.99	99.0±1.03
Group D2	98.7±1.12	98.9±0.90	98.6±1.25	98.8±1.14	98.9±1.31	98.9±1.28

Table 6 Comparison of Icc Score, Paed Score and Phbq Case in 3 Groups

Groups	ICC	PAED	PHBQ(Y/N)
Group C	4.9±1.7	13.3±2.2	16/14
Group D1	2.6±1.1*	7.8±3.1*	6/24*
Group D2	2.4±0.7*	7.4±3.3*	5/25*

No regurgitation aspiration, laryngospasm, bucking, labored breathing, vomiting, apnea, and other adverse reactions were observed in the pediatric patients of the three groups during the perioperative period.

4. Conclusion

The pediatric patients undergoing laparoscopic high ligation for incarcerated inguinal hernia are mostly preschool children. Children in this period are superior in subcortical central activities with relatively poor emotional management capability and varied and unstable emotion. Preschool period is an important period for psychological growth and emotional development of children. Mental health care of pre-school children is an issue to be concerned by medical staff. There was no significant difference in the general data of the three groups in this study. The research objects selected by this study were balanced and comparable. The scores of this study were evaluated by nurse anesthetists uninformed of the group division.

Published by Kain in 1998, the induction period cooperation table is adopted to evaluate the cooperative level during anesthesia induction of children, which is divided into 11 items with 0-10 scores each. The negative behaviors of children in the induction period are scored from 10 scores (completely uncooperative) to 0 scores (perfectly cooperative). Each negative behavior in the

induction period is scored 1 score, and the total scores are obtained by summing up all the scores. The lower the score is, the higher the degree of anesthesia induction cooperation is.

Prepared by Sikich et al., the emergence delirium scale divides the behaviors in the recovery period into 5 items, with a score range from 0 to 4 scores. The higher the score is, the higher the agitation level is. PAED scale further increases the reliability of the assessment results and is specific for emergence delirium assessment of children.

The post-discharge behavior questionnaire is a widely adopted tool for measurement of post hospitalization behavior change, which includes six parts, i.e. overall anxiety, separation anxiety, sleep anxiety, eating disorders, aggressivity, apathy and withdrawal, totaling 27 items. Parents need to compare the behaviors of children before and after hospitalization. 0 score range = equivalent to the level before hospitalization, - 1 = with level lower than that before hospitalization, - 2 = with level lower than that before hospitalization, 1 = with level higher than that before hospitalization, 2 = with level higher than that before hospitalization. If the total scores exceed 0 score, it means the occurrence of post hospitalization behavior change.

After the combination of Dex and α_2AR, restrain the release of noradrenaline by sympathetic nerve endings and reduce the plasma concentration. In central nervous system, Dex mainly acts on the occipital horn presynaptic and intermediate neurons postsynaptic membrane receptors in the hypothalamus, the medulla oblongata and the spinal cord, and plays a pharmacological role in combination with α_2AR distributed in locus coeruleus of brainstem. The sedative-hypnotic status incurred thereby is similar to natural sleep. Dex acts on the receptor of spinal cord and produces analgesic effect. Dex has little inhibitory effect on respiratory center {Sottas, 2017 #146}. Other effects of Dex include diuresis, shivering reduction, glandular secretion reduction, neuron protection and heart protection. The hypotensive effect of Dex is consistent with the decrease of norepinephrine concentration in the blood, and not related to plasma renin activity and aldosterone concentration. Dex has a sedative and analgesic effect with little effect on the circulatory and respiratory functions, which can also inhibit the increase of plasma catecholamine concentration incurred by stress stimulation, and reduce the restlessness after inhalation of sevoflurane anesthesia. Dex has been attracting attentions increasingly in the field of pediatric anesthesia due to its unique pharmacological characteristics.

Transnasal administration is a relatively non-invasive simple administration method, which absorb drug into blood for circulation through the nasal mucosa, with fast onset of action, no first-pass effect, no stimulation to gastrointestinal tract, low coordination requirements and easy tolerance. It is especially suitable for premedication of pediatric patients anesthesia. According to the research by Bhat [4] et al., Dex (1 $\mu g \cdot kg^{-1}$) intranasal drop can provide satisfying sedative effect and reduce emergence delirium. The research by Xu [5] et al. believe that Dex (2 $\mu g \cdot kg^{-1}$) nasal spray has a satisfactory sedative effect on children premedication. As investigated by Li [6] et al., the effect of Dex intranasal drop is the same as that of nasal spray. The research by Tsiotou [7] et al. suggests that Dex (1 $\mu g \cdot kg^{-1}$) can reduce the occurrence rate and intensity of emergence delirium in pediatric patients undergoing tonsillectomy with propofol anesthesia. Dex intranasal drop (1 or 2 $\mu g \cdot kg^{-1}$) can improve the mask acceptance level of sevoflurane anesthesia during pediatric patient induction, and reduce the emergence delirium, without extending the recovery time or serious adverse effects [8]. As found by this study, compared with group C, the ICC scores, PAED scores and PHBQ cases in group D1 and group D2 decreased significantly ($P < 0.05$); there was no significant statistical difference between group D1 and group D2 ($P > 0.05$). It shows that the premedication of Dex 1 $\mu g \cdot kg^{-1}$ and Dex 2 $\mu g \cdot kg^{-1}$ intranasal drops can significantly increase the cooperation degree of anesthesia induction, and decrease the occurrence of emergence delirium and postoperative behavior changes; compared with Dex 2 $\mu g \cdot kg^{-1}$, Dex 1 $\mu g \cdot kg^{-1}$ has no difference on the cooperation degree of anesthesia induction, emergence delirium and postoperative behavior changes.

Medulla oblongata and locus coeruleus are important binding points of Dex in central nervous system, which are related to haemodynamics and sedative and hypnotic effects respectively [9]. High dose or rapid intravenous infusion of Dex may incur transient heart rate decrease and blood pressure

rise. Dex acts on α_{2B}AR in the subsynaptic membrane of vascular smooth muscle, causing vasoconstriction. When the load dosage is reduced or the administration time is ＞10 minutes, presynaptic membrane α_{2B}AR is excited, adrenaline is released, sympathetic nerve conduction is inhibited, vagus nerve is enhanced, and blood pressure and heart rate are slowly decreased [10]. As found by this study, compared with T0, group C and group D1, MAP and HR of group D2 decreased significantly ($P < 0.05$). The results showed that Dex 1 $\mu g \cdot kg^{-1}$ intranasal drop had no effect on MAP and HR, and Dex 2 $\mu g \cdot kg^{-1}$ intranasal drop reduced MAP and HR significantly. However, MAP and HR decreases were within the acceptable range without adverse reactions. Dex had a slight effect on respiration {Tsuzawa, 2015 #145}. As found by this study, compared with T0, group C and group D1, the difference of SpO2 in group D2 had no statistical significance ($P > 0.05$). The results showed that Dex 1 $\mu g \cdot kg^{-1}$ and Dex 2 $\mu g \cdot kg^{-1}$ had no effect on SpO2.

No regurgitation aspiration, laryngospasm, bucking, labored breathing, vomiting, apnea, and other adverse reactions were observed in the pediatric patients of the three groups during the perioperative period.

In conclusion, Dexmedetomidine preoperative intranasal drop 1 $\mu g \cdot kg^{-1}$ in children undergoing laparoscopic high ligation for incarcerated inguinal hernia can increase anesthesia induction compliance, decrease emergence delirium and post hospitalization behavior change, with no obvious adverse reaction. Compared with Dex 1 $\mu g \cdot kg^{-1}$, the incidence rate for anesthesia induction compliance, emergence delirium and post hospitalization behavior change of Dex 2 $\mu g \cdot kg^{-1}$ had no difference, but MAP and HR decreased significantly.

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