

Comparative Study and Safe Dose Analysis of Dexmedetomidine in the Prevention of Emergence Agitation and Emergency Delirium in Children Undergoing General Anesthesia

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Abstract: The purpose of this paper is to explore the safe and effective dose of dexmedetomidine for the prevention of agitation and delirium during the awakening period for children undergoing general anesthesia. Samples of 989 cases are collected from children with comprehensive treatment of dental caries, and were randomly divided into four groups. Group A, group B and group C were intravenously at constant speed (60 mL/h), 0.5 and 0.25 infusion with 1 $\mu\text{g/kg}$ dexmedetomidine. Group D (control group) was intravenously saline at the same speed. The score of 5-point scale and the incidence of ED (emergency delirium) and EA (emergence agitation) in four groups were compared. Comparison of four groups of CHIPPS (children and infants postoperative pain) score, the amount of operation time and record seven halothane (TO), time to stop cover drug withdrawal of laryngeal anesthesia (TM), eye opening time (TE), independent records of children at the time of ICU stay after anesthesia (TP). Results show that there was no significant difference between the four groups ($p > 0.05$), among which the TM in B, C groups was significantly higher than that in A, D groups ($p < 0.05$). Group C was significantly higher than group B ($p < 0.05$). There was no significant difference in TE and TP between the A, B, D groups ($p > 0.05$). TE in group C was significantly higher than that in groups A, D ($p > 0.05$). The TP of group C was significantly higher than that of groups A, D ($p < 0.05$), but there was no significant difference between the B, C groups ($p > 0.05$). The incidence rates of EA and ED in groups A and B were significantly lower than those in group D ($p < 0.05$). Group C was significantly lower than group A ($p < 0.05$). There was no significant difference between group C and group C ($p > 0.05$). The CHIPPS score and sevoflurane dosage in groups A and B were significantly lower than those in group D ($p < 0.05$). Group C was significantly lower than group A ($p < 0.05$). There was no significant difference between group C ($p > 0.05$). Conclusion: the dose of dexmedetomidine 0.5 $\mu\text{g/kg}$ in children with general anesthesia can prevent restlessness and delirium after operation.

Key words: Children's general anesthesia, dexmedetomidine, emergence agitation, emergency delirium.

1. Introduction

In pediatric anesthesia, postoperative agitation (EA (emergence agitation) and ED (emergency delirium)) delirium is a common adverse reaction [1]. The anesthesia recovery period after EA is a kind of consciousness disorder, the specific performance for the state of consciousness and behavior of separation, with excitement, irritability and disorientation etc. [2]. ED is a transient disturbance of consciousness, mainly manifested as decreased perception of surrounding

environment, combined with the disorientation and perception of change [3]. ED can occur in the postoperative anesthesia recovery stage, time sustainable few minutes and several hours, the duration of ED has a direct impact on children after anesthesia of mental state and mental recovery [4]. The pathogenesis of ED is not completely clear, and may be related with age, pain, narcotic drugs and other factors related [5], at the same time, a study [6] shows that as a drug commonly used in pediatric general anesthesia can be seven halothane, the probability of ED increased significantly after anesthesia in children, so that children with behavior

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performance in a trance, directional force difference even the spirit of EA or radical, hindered the postoperative patients with mental condition. Dexmedetomidine mainly through the central and peripheral α_2 adrenergic receptor exerts its hypnotic and analgesic sedative and anxiolytic effects [7]. Research shows that dexmedetomidine can reduce the occurrence of ED after general anesthesia in children, further study [8] pointed out that dexmedetomidine also can reduce the effect of EA and ED after surgery in pediatric general anesthesia, but the safe and effective dose of dexmedetomidine to prevent children general anesthesia ED is not completely clear. The aim of this study is to observe the safety and effective dose of dexmedetomidine in preventing children's EA and ED during the general anesthesia recovery period by observing different doses of dexmedetomidine during the observation of children undergoing comprehensive treatment of dental caries under general anesthesia. Sevoflurane is widely used in pediatric anesthesia for its pharmacological profile, which allows rapid inhalational induction and awakening from anesthesia, low hepatotoxicity and hemodynamic stability. However, the occurrence of agitation is a common phenomenon in children undergoing general anesthesia with sevoflurane [9]. Emergence agitation in children was first described in the early 1960s and is characterized by a dissociated state of consciousness in which the child becomes inconsolable, irritable, uncooperative, and sometimes aggressive. Although temporary, it is an extremely distressing event for children, parents, and health professionals [10].

Prevalence of agitation varies from 25% to 80% in the literature, depending on the definition and criteria used by the authors [11]. It is influenced by the technique and anesthetic agents [12]. Different drugs such as opioids, ketamine, benzodiazepines, and α_2 -agonists, have been used in the prevention and treatment of agitation, but with varying success, which contributes to the development of studies to improve

perioperative care delivered to children.

Dexmedetomidine is a highly selective α_2 -adrenergic, with $\alpha_2:\alpha_1$ receptor ratio of 1,600:1, and has important sedative and analgesic effects [13]. Its sedative effect occurs through inter-action with postsynaptic α_2 -receptors in the locus coeruleus, reduces noradrenalin release, and facilitates the action of inhibitory neurons, particularly gamma-aminobutyric acid system. The analgesic effect is promoted by the action of α_2 -receptors on dorsal horn and supraspinal cord [14].

2. Methods

2.1 Materials

A total of 989 children with comprehensive general anesthesia for caries in our hospital from July 2016 to July 2017 were selected. Inclusion criteria: (1) ASA grade I-II; (2) the age of 1~10 years old; (3) weight greater than 10 kg; (4) with uncooperative children; (5) the informed consent and signed informed consent. Exclusion criteria: (1) children with respiratory infection history within 1 week; (2) children with congenital malformations such as congenital heart disease; (3) children with mental abnormalities; (4) children who used sedatives or analgesics for a long time; (5) children with severe liver and kidney dysfunction. These 989 patients are divided by treatment sequence number, obtained from the random number table of random numbers, each number corresponding to 1 random number, random numbers in ascending order will, according to the order of groups A, B, C and D, the grouping scheme with an opaque envelope, the envelope number marked on the outside.

2.2 Surgical Anesthesia and Drug Use

The dental caries comprehensive treatment for all the children was completed by a doctor with a deputy chief physician. The fasting time was 8 hours before the operation, and no drinking was 4 hours. There was no preoperative anesthetic medication. After opening

the peripheral vein, it was put into the operation room. Methods of anesthesia: intravenous injection of midazolam 0.1 mg/kg, fentanyl 2.5 µg/kg, propofol 2.5 mg/kg, 0.1 mg/kg atracurium as the induction, induction of anesthesia successfully was implanted into the laryngeal mask anesthesia machine, with mechanical ventilation (pressure control in 9~18 cm H₂O), respiratory rate from 18 to 25/min, respiratory ratio of 1:1.5~2, maintain PetCO₂ (end-tidal carbon dioxide) in 35~45 mm Hg inhalation of seven halothane (70% for oxygen: 30% air, 2 L/min) to maintain anesthesia. Then children in groups A, B and C were injected with different doses of dexmedetomidine (0.25, 0.5 and 1 µg/kg respectively) by intravenous constant speed (60 mL/h), and D group (control group) was pumped into normal saline at the same speed. Intraoperative fluid for infusion of lactated Ringer's solution, the speed of 10 mL/(kg·h), at the same time monitoring of children with ECG (electrocardiography), oxygen saturation (SpO₂), HR (heart rate), MAP (mean arterial pressure) and PaCO₂ (carbon dioxide partial pressure), sevoflurane concentration regulation during HR MAP and smooth, 5 min before surgery to stop medication, stay children with spontaneous breathing recovery of removing laryngeal mask airway.

2.3 Evaluating Indicator

Main outcome measures: the 5-point scale EA and ED degree within 2 h after operation (the evaluation score of 1 to 5, corresponding to quiet sleep, awake, calm, irritability, crying, can be calm, is not to appease the crying). The incidence of ED and EA during the awakening period of the 4 groups was compared. To

end point: the children and infants postoperative pain score within 2 h after operation (CHIPPS) scale.

2.4 Statistical Method

Statistical analysis of the data was performed using SPSS 22 statistical software, count data were expressed as a percentage, and compared with χ^2 test, measurement data of normal distribution was expressed in $\bar{x} \pm s$, non-normal distribution of measurement data used the median (four percentile interval), normal distribution data were analyzed by variance analysis, a further 22 compared with the SNK test, non-normal distribution data were compared among groups using Kruskal Wallis test, $p < 0.05$, the difference was statistically significant.

3. Result

3.1 Comparison of the General Data for Four Groups' Children

There was no significant difference in age, weight, sex ratio and the proportion of unilateral and bilateral hernia in the 4 groups ($p > 0.05$) (see Table 1).

3.2 Comparison of Anesthesia Time for Four Groups' Children

There was no significant difference between the four groups of children with TO ($F = 1.657$, $p = 0.245$), there was statistical significance difference between the four groups of children with TM ($F = 7.248$, $p = 0.011$), in which groups A, B and C were significantly higher than that of group D ($p < 0.05$). Group C was significantly higher than that of group B ($p < 0.05$). The four groups had statistical significance in the difference of TE ($F = 13.452$, $p = 0.001$), which was

Table 1 Comparison of general data of four groups' children.

Group	Number of cases	Age (month)	Weight (kg)	Gender	
				Male	Female
A	240	24 ± 11	13.94 ± 2.46	115	125
B	240	25 ± 10	13.62 ± 2.51	120	120
C	240	26 ± 12	13.31 ± 2.73	130	110
D	240	25 ± 10	13.77 ± 2.66	120	120

Table 2 Comparison of anesthesia time for four groups' children.

Group	Number of cases	TO (min)	TM (min)	TE (min)	TP (min)
A	240	25.23 ± 7.24	2.84 ± 0.46	8.84 ± 1.46	12.84 ± 2.46
B	240	24.19 ± 6.87	3.56 ± 0.51	9.56 ± 1.51	17.56 ± 3.51
C	240	25.17 ± 6.69	4.14 ± 1.73	12.14 ± 2.73	19.14 ± 4.73
D	240	24.87 ± 7.51	2.56 ± 0.66	8.56 ± 1.56	16.56 ± 2.66

Table 3 Comparison of the degree of EA and ED in four groups' children.

Group	Number of cases	Average scores	EA	ED
A	240	3 (2,4)	2.84 ± 0.46	8.84 ± 1.46
B	240	2 (1,2)	3.56 ± 0.51	9.56 ± 1.51
C	240	1 (1,2)	4.14 ± 1.73	12.14 ± 2.73
D	240	3 (3,4)	2.56 ± 0.66	8.56 ± 1.56

not statistically significant in groups A, B and D. The difference between the three groups ($p > 0.05$). Group C was significantly higher than that of groups A, B and D ($p < 0.05$). By comparison of children with TP, there were significant differences between the four groups ($F = 11.223$, $p = 0.002$), no statistical significance of groups A, B and D, the difference between the three groups ($p > 0.05$), group C was significantly higher than that of groups A and D ($p < 0.05$), and no significant difference between groups B and C, the difference between the two groups ($p > 0.05$) (see Table 2).

3.3 Comparison of the Degree of EA and ED in Four Groups' Children

The median score of group A was 3, group B was 2, group C was 1, group D was 3, there was significant difference between four groups, in which A, B, C three groups were significantly lower than that of group D ($p < 0.05$). Groups B and C were significantly lower than group A ($p < 0.05$). There was no significant difference between groups B and C ($p > 0.05$). Four groups of children with EA and ED incidence were statistically significant (" 2 " = 25.116, $p < 0.001$; " 2 " = 28.341, $p < 0.001$), in which groups A, B, C three groups were significantly lower than that of group D ($p < 0.05$), while groups B and C were significantly lower than group A ($p < 0.05$), there was no significant difference between groups B and C ($p > 0.05$) (see Table 3).

4. Conclusions

ED is a transient disturbance of consciousness, which can be associated with EA, hallucination and discontinuity of thinking. It is a disturbance of perception and attention to the surrounding environment, accompanied by directional disability and perceptual change. In this study, by comparing the different group of dexmedetomidine dose, respectively 0.25 g/kg, 0.5 g/kg and 1 g/kg, three dosing regimens, for pediatric patients, the dose group foreign the dosage of dexmedetomidine in preventing EA were studied, and the maximum dose of drug instructions was grouped. The general data of four groups of children in random groups showed good homogeneity. Although there was no significant difference in operation time of the four groups, but difference between groups B and C of narcotic drugs to stop pulling the laryngeal mask was significantly higher than that of groups A and D. Group C was significantly higher than that of group B. Groups A, B and D were independent open time difference that was not statistically significant, while group C was independent open your eyes was obviously prolonged, it showed that the use of dexmedetomidine, children with recovery time and extubation time, because children recover faster, and the recovery time of central differences, the use of dexmedetomidine will help promote consistency and recovery of central recovery, the results of this study are consistent with domestic

similar findings. The time needed for the stay in the ICU after anesthesia (TP) is the longest in group C, which indicates that the time needed for postoperative monitoring is prolonged when the dosage of drugs is large. Therefore, this indicates that the dose of 0.5 g/kg increases the time of the child to wake up and the laryngeal mask, but does not prolong it.

Comparison of four groups of children with EA and ED, groups B and C were the 5-point scale and EA, ED compared the incidence is lower than that of groups A and D, while the patients in the group A were 5-point scale and EA, the incidence of ED was also lower than that of group D, but further increase dosage to 0.5 g/kg children, can further reduce the occurrence of EA and ED. Compared with the group C using 1 g/kg dose of patients, group B was 5-point scale and EA, ED have no significant differences in the incidence, it shows that the 0.5 g/kg dose reached EA and prevention of anesthesia recovery period ED, although studies have pointed out that it is the same with propofol and fentanyl with the prevention of the role of EA, the use of the four groups of children with basic anesthesia scheme. To evaluate the effect of dexmedetomidine in preventing EA and ED results are more reliable. However, dexmedetomidine itself has a certain effect on hemodynamics. The dosage of seven halothane also needs to be adjusted according to hemodynamics.

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