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Original Article

Effects of dexmedetomidine on the prevention of nausea and vomiting in children after upper limb fracture surgery

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Abstract: Objective: To investigate the effect of dexmedetomidine on the prevention of postoperative nausea and vomiting (PONV) in children undergoing upper limb fracture surgery. Methods: A total of 82 children undergoing upper limb fracture surgery were divided into either a control group, which received general anesthesia plus brachial plexus block, or a study group, which received additional dexmedetomidine. The incidence of nausea and vomiting, postoperative agitation, perioperative hemodynamic parameters, stress-related indicators, Visual Analogue Scale (VAS) scores, and perioperative conditions were compared between the two groups. Results: The incidences of nausea and vomiting, postoperative agitation, and the postoperative VAS scores were significantly lower in the study group than in the control group. Compared with baseline values at T0, the levels of malondialdehyde, norepinephrine, epinephrine, and cortisol increased in both groups; however, these increases were significantly lower in the study group than in the control group. In addition, the onset time of anesthesia, awakening time, and post-anesthesia care unit (PACU) stay were all shorter in the study group than in the control group. Conclusions: The use of dexmedetomidine in children undergoing upper limb fracture surgery can attenuate perioperative hemodynamic fluctuations and stress reactions, alleviate postoperative pain, shorten awakening time, and reduce the incidence of postoperative nausea and vomiting.

Keywords: Dexmedetomidine, fracture, nausea and vomiting

Introduction

The number of pediatric orthopedic surgeries continues to increase due to insufficient safety awareness and limited self-protection abilities in children. Ensuring the safety and effectiveness of anesthesia remains a challenging and important clinical concern [1]. Due to the psychological and physiological characteristics of children, general anesthesia or nerve block combined with intravenous anesthesia is mostly used in surgery. General anesthesia often requires tracheal intubation, which increases the risk of respiratory depression and prolongs the duration of stay in the post-anesthesia care unit (PACU). Ketamine, a commonly used anesthetic in nerve block combined with intravenous anesthesia, is associated primarily with adverse effects such as nausea and vomiting. At the same time, high doses can induce excessive respiratory secretion, prolong awakening period, and even cause delirium or other postoperative complications, thereby reducing perioperative tolerance in children [2, 3]. Dexmedetomidine (Dex), an α2-adrenoceptor agonist, reduces the release of norepinephrine by inhibiting sympathetic neuronal firing, leading to its analgesic and sedative effects. Unlike many other anesthetics, Dex does not cause respiratory depression, making it particularly useful for maintaining hemodynamic stability during anesthesia [4-6]. However, the clinical efficacy of Dex in preventing postoperative nausea and vomiting (PONV) in children after fracture surgery has not been extensively validated. Therefore, the present retrospective analysis included 82 children with fractures admitted to our hospital to evaluate the clinical efficacy of Dex in preventing PONV.

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Materials and methods

General information

This retrospective analysis included 82 children with upper limb fractures admitted to our hospital between March 2019 and November 2020. Patients were divided into a control group (n = 41, receiving general anesthesia combined with brachial plexus nerve block) and a study group (n = 41, receiving additional Dex on the basis of control group) based on the anesthesia regimen they received.

Inclusion criteria: (1) Diagnosis of upper limb fracture confirmed by CT or other imaging examinations; (2) American Society of Anesthesiologists (ASA) grade I-II [7]; (3) School-age children (6-13 years old); (4) Clear consciousness; (5) Stable vital signs; (6) Normal skeletal and intellectual development.

Exclusion criteria: (1) Allergic constitution; (2) History of allergy to the study drug; (3) Presence of renal or hepatic lesions; (4) Presence of atrioventricular block, bradycardia, or congenital heart disease; (5) Presence of respiratory system diseases.

The study protocol was reviewed and approved by the Medical Ethics Committee of Mianyang 404 Hospital (No. 2019-012). Due to the retrospective nature of this study, patient informed consent was therefore waived by the Ethics Committee.

Methods

Preoperative assessments, including electrocardiogram, blood biochemistry, and X-ray examinations, were performed to clarify the type of fracture and formulate a surgical plan. In the control group, general anesthesia in conjunction with brachial plexus nerve block was administered. Anesthesia was induced using propofol (2.5-4 mg/kg; Corden Pharma S.P.A, AstraZeneca, UK) and sufentanil (0.2-0.3 ug/kg; Yichang Renfu, China), while the nerve block was performed using a mixture of ropivacaine (0.25%, Shandong New Times, China) and lidocaine (1%, Swiss American Chemical Pharmaceuticals). This combined approach was used to provide both general anesthesia and regional pain relief during surgery. Laryngeal mask general anesthesia used low-flow oxygen inhalation for 5 minutes. Once spontaneous respiration subsided, ventilation was switched to pure oxygen via a face mask. After the restoration of spontaneous respiration, semi-closed ventilation was initiated using an anesthesia machine, and anesthesia was maintained with continuous intravenous infusion of remifentanil (0.5-1 ug/kg.min; Yichang Renfu, China) and propofol (9-15 mg/kg·h). The brachial plexus nerve block was guided by a nerve stimulator, and the volume and concentration of the blocking solution were adjusted according to the child's vital signs, age, and weight.

The study group received dexmedetomidine intravenously additionally, on the basis of treatment given to the control group, with a loading dose of 0.5 μg/kg followed by a maintenance infusion of 0.4 μg/(kg·h).

Outcome measures

Primary outcome: The primary outcome was the incidence of PONV within 24 hours after surgery. PONV was defined as any episode of nausea or vomiting after surgery. The severity of PONV was graded as follows: grade 0, no nausea or vomiting; grade 1, mild nausea without vomiting; grade 2, nausea with occasional vomiting; and grade 3, severe vomiting. The incidence of PONV was calculated as the number of patients with grade 1-3 PONV divided by the total number of patients × 100%.

Secondary outcomes: (1) Hemodynamic and Stress-Related Indicators: heart rate (HR), mean arterial pressure, (MAP), and stress-related indicators (e.g., superoxide dismutase [SOD], malondialdehyde [MDA], norepinephrine [NE], epinephrine [E], cortisol [Cor]) were measured in both groups at preoperative (T0), 10 minutes after the start of surgery (T1), and immediately after surgery (T2).

(2) Postoperative Pain: Pain was assessed using the Visual Analogue Scale (VAS) at 1, 6, 12, and 24 hours after surgery. The VAS score ranges from 0 to 10 points, with higher scores indicating more severe pain.

(3) Perioperative Recovery Parameters: Operation time, onset time of anesthesia, awaken-

Table 1. Comparison of general information between the two groups

Group	Study group (n=41)	Control group (n=41)	χ^2/t	P
Sex (male/female)	22/19	26/15	0.804	0.370
Age (years)	9.6±2.4	10.0±2.5	0.852	0.397
ASA classification			0.467	0.494
Grade I	24	27		
Grade II	17	14		
Affected side			0.456	0.499
Left	15	18		
Right	26	23		
Weight (kg)	25.06±6.11	23.98±5.67	0.830	0.409

Note: ASA, the American Society of Anesthesiologists.

Table 2. Comparison of the incidence of PONV between the two groups (n, %)

Group	Cases	Grade 1	Grade 2	Grade 3	Total incidence rate
Study group	41	2 (4.88)	1 (2.44)	1 (2.44)	4 (9.76)
Control group	41	7 (17.07)	2 (4.88)	2 (4.88)	11 (26.83)
χ^2					3.998
P					0.046

Note: PONV, postoperative nausea and vomiting.

ing time, and post-anesthesia care unit (PACU) stay time were recorded for both groups.

(4) Postoperative Emergence Agitation: Emergence agitation was evaluated using the Pediatric Anesthesia Emergence Delirium (PAED) scale at 10, 20, and 30 minutes after admission to the PACU [8]. The PAED scale consists of five items, each scored 0-4, yielding a total score of 0-20; higher scores indicate more severe emergence agitation. The highest PAED score recorded during PACU stay was used for analysis. Emergence agitation was defined according to the prespecified PAED cut-off value, and its incidence was calculated as the number of patients with emergence agitation divided by the total number of patients × 100%.

Statistical analyses

Statistical analysis was performed using SPSS 22.0. The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. Normally distributed continuous variables were expressed as mean ± standard deviation (SD), whereas non-normally distributed variables were expressed as median and interquartile range (IQR). For normally distributed continuous variables measured at a single time point, comparisons between groups were performed using the independent samples t-test. For repeated-measures variables, including hemodynamic indicators, stress-related indicators, and VAS scores, repeated-measures analysis of variance was used to evaluate the effects of group, time, and group-by-time interaction. When significant effects were observed, Bonferroni correction was applied for post-hoc comparisons. Categorical variables, including the incidence of PONV and postoperative agitation, were expressed as n (%) and compared using the chi-square test or Fisher's exact test as appropriate. A two-tailed *P* value < 0.05 was considered statistically significant.

Results

General information

All continuous variables included in the parametric analyses were normally distributed according to the Kolmogorov-Smirnov test (all P > 0.05). There were no significant differences between the study group and the control group in sex, age, ASA classification, affected side, or weight (all P > 0.05; **Table 1**).

Postoperative nausea and vomiting (PONV)

The incidence of PONV in the study group (9.76%) was significantly lower than that in the control group (26.83%) (P < 0.05; **Table 2**).

Hemodynamic indicators

At baseline (T0), there were no significant differences in HR or MAP between the two groups (all P > 0.05). Repeated-measures ANOVA

Table 3. Comparison of hemodynamic indicators between the two groups ($\bar{x}$ ± sd)

Group	Cases	T0	T1	T2
HR (per/min)				
Study group	41	91.67±5.91	96.97±6.22*	100.64±7.19*
Control group	41	89.56±6.13	101.78±8.06*	110.38±6.44*
t		1.587	3.029	6.506
P		0.117	0.003	< 0.0001
MAP (mmHg)				
Study group	41	72.37±4.59	80.11±7.66*	83.93±6.55*
Control group	41	74.01±6.09	93.39±9.06*	95.57±7.79*
t		1.377	7.167	7.323
P		0.172	< 0.0001	< 0.0001

Note: Compared with T0, *P < 0.05. HR: heart rate; MAP: mean arterial pressure.

Table 4. Comparison of stress-related indicators between the two groups ($\bar{x}$ ± sd)

Group	Cases	T0	T1	T2
E (ng/L)				
Study group	41	46.09±6.64	57.51±8.32*	63.11±10.13*
Control group	41	44.32±5.81	69.71±10.20*	80.86±13.18*
t		1.285	5.935	6.837
P		0.203	< 0.0001	< 0.0001
NE (ng/L)				
Study group	41	228.64±26.51	280.13±33.65*	315.36±39.74*
Control group	41	232.73±30.45	378.26±41.81*	446.59±50.22*
t		0.649	11.708	13.121
P		0.518	< 0.0001	< 0.0001
Cor (μg/L)				
Study group	41	31.38±2.96	35.69±3.11*	37.74±2.09*
Control group	41	32.05±3.14	40.81±3.29*	41.44±4.02*
t		0.994	7.241	5.229
P		0.323	< 0.0001	< 0.0001
MDA (nmol/L)				
Study group	41	81.38±4.69	92.29±8.00*	95.61±8.38*
Control group	41	79.91±5.04	101.35±9.61*	105.44±10.08*
t		1.367	4.639	4.802
P		0.175	< 0.0001	< 0.0001
SOD (μmol/L)				
Study group	41	109.46±9.53	93.14±6.63*	88.03±5.59*
Control group	41	111.13±10.89	82.68±9.01*	79.92±5.44*
t		0.739	5.987	6.658
P		0.462	< 0.0001	< 0.0001

Note: Compared with T0, *P < 0.05. E: epinephrine; NE: norepinephrine; Cor: cortisol; MDA: malondialdehyde; SOD: superoxide dismutase.

showed significant effects of time and group-by-time interaction for HR and MAP. Post-hoc comparisons showed no significant differences at T0; however, HR and MAP were significantly lower in the study group than in the control group at T1 and T2 (**Table 3**).

Stress response related indicators

There was no significant difference in the baseline levels of SOD, MDA, NE, E, and Cor between the two groups at T0 (P > 0.05). Repeated-measures ANOVA showed significant time effects and group-by-time interaction effects for SOD, MDA, NE, E, and Cor. Post-hoc comparisons showed that SOD decreased after surgery, whereas MDA, NE, E, and Cor increased after surgery in both groups; however, these stress-related changes were less pronounced in the study group than in the control group (**Table 4**).

VAS scores

Preoperative VAS scores were comparable between the two groups (P > 0.05). Repeated-measures ANOVA showed significant time effects and group-by-time interaction effects. Post-hoc analysis indicated that VAS scores at postoperative 1, 6, 12, and 24 hours were significantly lower in the study group than in the control group (all P < 0.001, **Table 5**).

Perioperative conditions

There was no significant difference in operation time between the two groups (P > 0.05). However, the anesthesia onset time, awakening time, and PACU stay in the study group were significantly shorter than those in the control

Table 5. Comparison of VAS scores between the two groups ($\bar{x}$ ± sd)

Group	Cases	1 hour after surgery	6 hours after surgery	12 hours after surgery	24 hours after surgery
Study group	41	2.36±0.69	1.95±0.44	1.79±0.40	1.60±0.34
Control group	41	3.23±1.01	2.46±0.56	2.38±0.50	2.01±0.42
t		4.554	4.585	5.900	4.858
P		< 0.0001	< 0.0001	< 0.0001	< 0.0001

Note: VAS: Visual Analogue Scale.

Table 6. Comparison of perioperative conditions between the two groups ($\bar{x}$ ± sd)

Group	Cases	Operation time (min)	Anesthesia onset time (min)	Awakening time (min)	PACU stay (min)
Study group	41	119.28±13.95	3.10±0.73	5.69±1.45	11.69±3.18
Control group	41	124.05±15.65	3.71±0.96	9.30±3.06	20.04±6.09
t		1.457	3.239	6.826	7.782
P		0.149	0.002	< 0.0001	< 0.0001

Notes: PACU, post-anesthesia care unit.

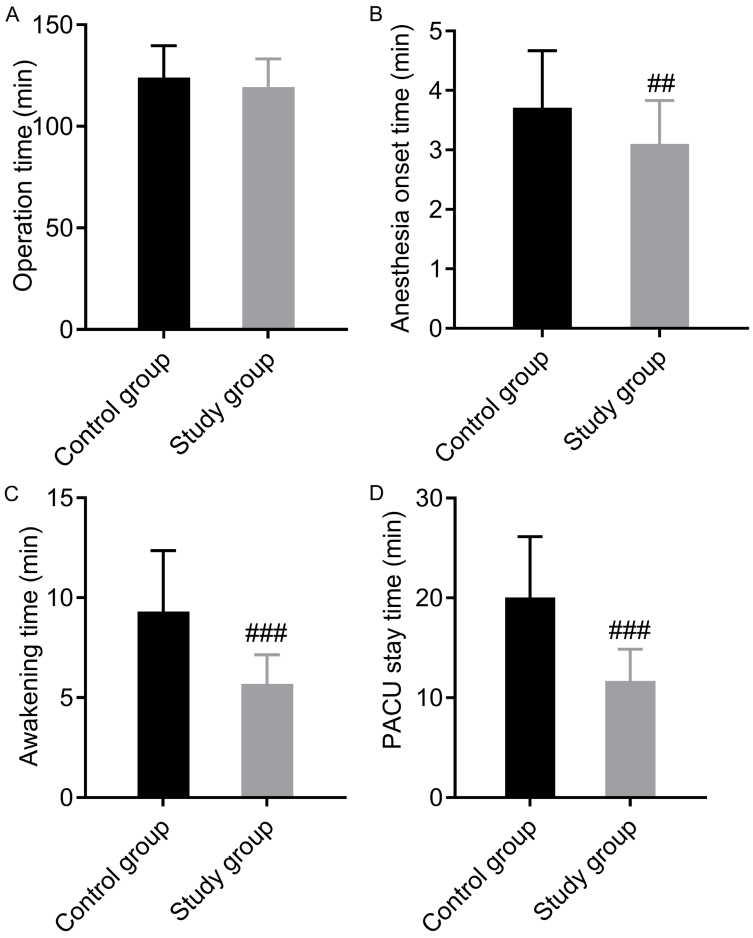

Figure 1. Comparison of perioperative conditions between the two groups. A: Operation time; B: Anesthesia onset time; C: Awakening time; D: PACU stay. Notes: PACU, post-anesthesia care unit. Compared with the control group, ##P < 0.01, ###P < 0.001.

group (all P < 0.01; **Table 6** and **Figure 1**).

Incidence of postoperative agitation

The incidence of postoperative agitation in the study group was significantly lower than that in the control group (P < 0.05, **Table 7**).

Discussion

Children with fractures are more challenging to anesthetize due to their young age, and it is difficult to balance the anesthetic effect and safety. Considering the characteristics of pediatric patients, general anesthesia is commonly applied during surgery. Although general anesthesia can achieve satisfactory operative conditions, it is associated with higher incidence of adverse reactions [7, 9].

Dex exhibits anxiolytic and central antisympathetic effects. It enters the bloodstream through microcirculation and selectively acts on α2-adre-

Table 7. Comparison of the incidence of postoperative agitation between the two groups (n, %)

Group	Cases	Mild postoperative agitation	Moderate postoperative agitation	Severe postoperative agitation	Total incidence rate
Study group	41	2 (4.88)	2 (4.88)	1 (2.44)	5 (12.20)
Control group	41	7 (17.07)	4 (9.76)	2 (4.88)	13 (31.71)
χ^2					4.556
P					0.033

nergic receptors to inhibit injurious neurotransmitter release, thereby enhancing central analgesic and sedative functions [10, 11]. Moreover, α2-adrenergic receptors are mainly distributed in vascular smooth muscle, such as in the kidney, allowing rapid metabolism and excretion, which contributes to its safety profile [12]. Shangguan et al. showed that Dex can maintain hemodynamic stability and shorten postoperative awakening time [9]. He et al. confirmed that combining Dex with conventional anesthesia in children undergoing upper limb fracture surgery can stabilize perioperative vital signs, enhance analgesic and sedative effects, and shorten the recovery process [13].

In this comparison, the study group exhibited more favorable hemodynamic and stress-related indicators compared with the control group. Furthermore, postoperative VAS scores were lower, anesthesia onset and awakening times were shorter, and the incidence of postoperative agitation was reduced in the study group compared to the control group. These findings suggest that Dex can attenuate perioperative hemodynamic fluctuations and stress responses, facilitate smooth operation, shorten awakening time, reduce pain, and prevent postoperative agitation in pediatric patients.

In addition, incidences of PONV are common adverse reactions after fracture surgery, which can prolong PACU stay and are a significant cause of unplanned postoperative hospitalization [14, 15]. In this study, the occurrence of PONV was lower in the study group than in the control group. Xu et al. reported that Dex reduced the incidence of PONV in patients undergoing laparoscopic total hysterectomy, consistent with the findings of the present study [16]. The underlying mechanisms may include a reduction in perioperative opioid need, decreased catecholamine release, reduced sympathetic excitability, and inhibition of the synthesis of norepinephrine [17-21].

A recent updated meta-analysis by Zhao et al. [22], which included 18 randomized controlled trials with 2,018 adult patients undergoing general anesthesia, demonstrated that Dex significantly reduced the incidence of PONV compared with controls (OR=0.49, 95% CI: 0.36-0.67). The meta-analysis also showed that Dex reduced perioperative opioid consumption, shortened extubation time and hospital stay, but increased the risk of bradycardia. These findings are consistent with our results, in which children receiving Dex exhibited a lower incidence of PONV. The possible mechanism may involve the opioid-sparing effect of Dex, inhibition of sympathetic activity, reduction of catecholamine release, and stabilization of perioperative hemodynamics.

This study does have some limitations. First, this study was a single-center study with a relatively small sample size. Second, the follow-up period was short. Therefore, multi-center, large-sample, long-term follow-up studies are warranted to confirm these findings.

Conclusion

In children undergoing fracture surgery, the use of dexmedetomidine as an adjunct to anesthesia can suppress perioperative hemodynamic fluctuations and stress reactions, reduce postoperative pain, shorten awakening time, and decrease the incidence of postoperative nausea and vomiting.

Disclosure of conflict of interest

None.

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