BMC Anesthesiology

RESEARCH

Open Access

Effect of preoperative dexmedetomidine administration on the bispectral index in children during sevoflurane inhalation anesthesia: a randomized controlled trial

Zhen Xiang[1†], Lei Wu[1†], Siwei Wei[1], Eryou Yu[1], Zheng Chen[1] and Zhen Du[1*]

Abstract

Background The available data on the effect of dexmedetomidine premedication on anesthesia depth in children during general anesthesia are limited. This study was designed to determine the effect of preoperative dexmedetomidine administration on the bispectral index (BIS) and sevoflurane requirements in children during sevoflurane anesthesia.

Methods 120 children aged 5 to 12 years undergoing concealed penis repair or hypospadias plastic surgery were randomized to receive preoperative administration of 0.25 μg kg^{-1} dexmedetomidine, 0.5 μg kg^{-1} dexmedetomidine, 0.75 μg kg^{-1} dexmedetomidine, or the same volume of placebo. The primary outcome was the change in the BIS value from before dexmedetomidine administration to 60 min after surgical incision. The secondary outcomes included the end-tidal sevoflurane concentration (ETsevo), hemodynamic data, anesthesia recovery data and intraoperative awareness.

Results Compared with those in Group C, the BIS values of children in Group D2 and Group D3 were significantly lower during sevoflurane induction and early maintenance ($P < 0.017$). Moreover, children in Group D2 and Group D3 had a lower ETsevo ($P < 0.001$) during sevoflurane maintenance than did those in Group C ($P < 0.017$). There were statistically significant differences in heart rate($P < 0.0001$) and mean arterial pressure($P < 0.001$) between the groups, but the incidence of bradycardia or hypotension was similar between the groups ($p = 0.779$ and $p = 0.901$).

Conclusions Children who received 0.5 μg kg^{-1} or 0.75 μg kg^{-1} dexmedetomidine preoperatively were more likely to achieve the target depth of anesthesia (BIS less than 60) during anesthesia induction and had lower BIS values during the early stage of anesthesia maintenance.

Trail registration The trial is registered with the China Clinical Trials Registry Registration Number: ChiCTR1900026872. Date of registration: 10/24/2019.

Keywords Dexmedetomidine, Anesthesia depth, Sevoflurane, Pediatric, Bispectral index

[†]Zhen Xiang and Lei Wu contributed equally to this work.

*Correspondence:
Zhen Du
meggyzhen@163.com

[1]Department of Anesthesiology, The Affiliated Children's Hospital of Xiangya School of Medicine, Central South University (Hunan Children's Hospital), Changsha, China

Introduction

In adult and pediatric anesthesia management, the depth of anesthesia monitoring is very important because it can not only reduce the occurrence of intraoperative awareness but also reduce the occurrence of delayed emergence and postoperative cognitive dysfunction [1, 2, 3]. Moreover, recent guidelines from the European Society of Anesthesiology and Intensive Care have similarly emphasized the importance of preoperative assessment and intraoperative monitoring in ensuring optimal anesthetic management [4]. Sevoflurane inhalation combined with a supraglottic airway is a safe and effective anesthesia technique widely used in pediatric surgery. Moreover, the bispectral index (BIS) has been validated in volunteers using agents that act predominantly at γ-aminobutyric acid–mediated (GABAergic) receptors, such as propofol, sevoflurane, isoflurane and midazolam [5]. The BIS is also widely used to monitor the depth of sevoflurane inhalation anesthesia in children [6, 7]. However, with the development of anesthetics, an increasing number of non-GABA receptor narcotic drugs, such as dexmedetomidine, are being widely used for clinical anesthesia, including pediatric anesthesia. This makes it challenging to monitor and predict the depth of anesthesia.

Dexmedetomidine is a highly specific α2-adrenergic receptor agonist that can produce stable sedative and awakening effects [8]. A study demonstrated that the combination of dexmedetomidine and sevoflurane may produce synergistic or enhancing effects on sedation levels and EEG performance in adults [9]. Moreover, in an adult study, premedication with dexmedetomidine significantly reduced the sevoflurane requirement during anesthesia induction and the initial phase of anesthesia maintenance [10]. Similarly, dexmedetomidine has been widely used in pediatric anesthesia. In our previous research, premedication with dexmedetomidine significantly reduced perioperative anxiety and postoperative inflammatory factor levels in children [11, 12]. Dexmedetomidine is also one of the few anesthetic aids used in children that does not cause cognitive impairment but has neuroprotective effects [13]. However, available data on the effect of dexmedetomidine premedication on anesthesia depth and sevoflurane requirements in children are limited. Hence, it is necessary to evaluate the effect of dexmedetomidine premedication on the depth of anesthesia in children.

To investigate this issue, we conducted a prospective, randomized, double-blinded study in which patients scheduled for concealed penis or hypospadias surgery were randomized to receive normal saline preoperatively or different doses of dexmedetomidine during sevoflurane anesthesia. The primary outcome was the change in the BIS value from before dexmedetomidine administration to 60 min after surgical incision. We hypothesized that children who received preoperative dexmedetomidine would have lower BIS values during anesthesia.

Methods

This was a prospective, single-center, parallel, randomized controlled trial performed between November 2019 and March 2020 according to the Declaration of Helsinki at the Affiliated Children's Hospital of Xiangya School of Medicine, Central South University (Hunan Children's Hospital). Ethical approval for this study (HCHLL-2019-10) was provided by the Ethics Committee of the Affiliated Children's Hospital of Xiangya School of Medicine, Central South University (also known as the Hunan Children's Hospital) (Chairperson Prof Zhenghui Xiao) on 28 April 2019. Before recruitment, the trial was registered at the Chinese Clinical Trial Registry website (ChiCTR1900026872). This study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline for randomized clinical trials.

Participants

Children aged 5–12 years who were scheduled to undergo concealed penis or hypospadias surgery at Hunan Children's Hospital were recruited. Patients were excluded if they used drugs that affect the circulatory system or block sympathetic response recently or before anesthesia induction, had an allergy to halogenated anesthetics, had contraindications for caudal block, or had mental retardation or neurological conditions. Potential participants were identified from the elective surgery list, and then a research team member contacted the parents or guardians of potential patients before surgery with a detailed explanation of the study aims and methods. All parents/guardians gave written informed consent for participation of their children in this study, and assent from the patient was sought when applicable.

Randomization and blinding

The children were randomly divided into a control group or different-dose dexmedetomidine groups, namely, Group C, Group D1 and Group D2 or Group D3. Randomization was performed by a statistician, and the data were concealed in sealed, opaque envelopes. The dexmedetomidine dose for each subject was prepared by an anesthesia nurse who did not participate in this study. The children and their family members, anesthesiologists and surgeons were blinded to the grouping. The procedures for all the subjects were performed by the same group of surgeons.

Anesthesia protocol

On the day of the operation, venous access was established under local anesthesia in the ward for all subjects, who entered the anesthesia induction room accompanied

by their parents. Anesthesia nurses fully communicated with the patients to relieve their tension and anxiety and then monitored basic indicators such as pulse oximetry, noninvasive blood pressure and ECG. At the same time, the electrodes of the bispectral index (BIS) monitor were accurately placed on the patient's forehead and connected to the monitor. After the completion of monitoring, drug administration was performed by an anesthesia nurse who was not involved in the study. Before inhalation with sevoflurane, the subjects were randomized to receive a continuous pump infusion of normal saline (Group C), 0.25 μg kg^{-1} dexmedetomidine (Group D1), 0.5 μg kg^{-1} dexmedetomidine (Group D2), or 0.75 μg kg^{-1} dexmedetomidine (Group D3). All drugs were diluted to 20 ml, and the continuous pumping time was 10 min. After the completion of administration with the drug, the inhalation of sevoflurane was induced through a mask. The sevoflurane vaporizer was opened to 8%, and the oxygen flow rate was 6 L min^{-1}. At the same time, the respiratory movement of the subjects was observed, and auxiliary respiration was applied if necessary. When the subjects lost consciousness (BIS value less than 60) and their mandibles relaxed, and the LMA was placed. Airway secretions were reduced with 0.1 mg kg^{-1} anisodamine hydrobromide during induction. Notably, no neuromuscular blocking agents and opioids were used during induction. After anesthesia induction, the children were turned to the left lateral position with their hips and knees flexed, and then a single caudal extradural injection of 1 ml kg^{-1} of 0.2% ropivacaine was performed under ultrasound guidance. During anesthesia maintenance, the anesthesiologist maintained a BIS value of 40 to 60 by adjusting the sevoflurane inhalation concentration. Similarly, other sedatives, neuromuscular blockers, and opioids were not used during the maintenance of anesthesia. During the operation, the end-expiratory carbon dioxide partial pressure was maintained between 35 and 45 mmHg. At the end of the operation, the inhalation of sevoflurane was stopped. The LMA was removed after the subject achieved better spontaneous respiration, and the subject was then transferred to the PACU. When the modified Aldrete scale score was ≥ 9, the subject was discharged from the PACU to the ward.

Clinical outcomes and assessments

The primary outcome was the change in the BIS values from before dexmedetomidine administration to 60 min after surgical incision. The time points at which data were recorded were as follows: the beginning of dexmedetomidine pumping (T0), the completion of dexmedetomidine pumping (T1), the end-tidal sevoflurane concentration (ETsevo) reaches 1% (T2), the ETsevo reaches 2% (T3), the ETsevo reaches 3% (T4), surgical incision (T5), 15 min (min) after surgical incision (T6), 30 min after surgical incision (T7), 45 min after surgical incision (T8), and 60 min after surgical incision (T9).

Secondary outcomes included the ETsevo at surgical incision (T5), 15 min after surgical incision (T6), 30 min after surgical incision (T7), 45 min after surgical incision (T8), and 60 min after surgical incision (T9); hemodynamic data included the mean arterial pressure (MAP) and heart rate (HR); PACU discharge time; and emergence time; and adverse events including bradycardia, hypotension, delayed emergence and intraoperative awareness. The outcome measures were as follows: PACU discharge time (time from PACU admission until a modified Aldrete scale score ≥ 9 was achieved); hypotension (a decrease in the mean arterial pressure from baseline of more than 30% for > 5 min); bradycardia (a decrease in the baseline heart rate of more than 20% for > 30 s); emergence time (time from cessation of anesthesia to discharge from the PACU); and delayed emergence (emergence time more than 2 h). The postoperative comfort score was measured with a numerical rating scale (NRS) ranging from 0 (extremely uncomfortable) to 10 (very comfortable).

Statistical analysis

In a pilot study of 32 children, the mean difference in the BIS value in each group was 54.1 (5.5), 52.1 (7.8), 49.5 (8.5), and 46.7 (6.3). Using a study power of 0.90 and an $\alpha = 0.05$, we calculated that 27 patients per group were required by using one-way analysis of variance (ANOVA). We planned to enrol 33 subjects per group to allow for patient withdrawal or exclusion.

Kolmogorov–Smirnov tests were used to test the normality of the data distribution. Normally distributed data and nonnormally distributed data are reported as the mean [standard deviation (SD)] and median (interquartile range [IQR]), respectively. Categorical data are presented as numbers (percentages). Normally distributed data were analyzed using one-way ANOVA with Tukey's post hoc test. Nonnormally distributed data were analyzed using the nonparametric Kruskal–Wallis test. When significant differences were found, the test was followed by three pairwise comparisons using the Mann–Whitney U test, and a p value < 0.017 (0.05/3) (Bonferroni adjustment for the three comparisons: Group D1 vs. Group C, Group D2 vs. Group C and Group D3 vs. Group C) was considered to indicate significance. Categorical data were analyzed using the chi-square test with Bonferroni correction. P values < 0.05 were considered to indicate statistical significance. Statistical analyses were performed using IBM SPSS Statistics 26.0 (SPSS Inc., Chicago, Illinois, USA).

Results

A total of 130 patients were screened in this study, and 120 patients completed the study. The study flowchart is shown in Fig. 1. Table 1 summarizes the baseline characteristics of the patients in each group. There were no significant differences between groups at baseline.

Figure 2 shows the BIS values for each group during the induction and maintenance of anesthesia. Before sevoflurane inhalation, intravenous injection of dexmedetomidine had no significant effect on the BIS value (T0, $P=0.543$; T1, $P=0.725$). During the induction of sevoflurane inhalation anesthesia, children pretreated with dexmedetomidine had lower BIS values. The median BIS values of patients in Group C, Group D1, Group D2 and Group D3 at T2, T3 and T4 were as follows: 88.0 (85–89) vs. 86.0 (83.8–88.3) vs. 81.0 (75.8–84.3) vs. 74.5 (70.3–76.3) ($p<0.0001$); 75 (69.0–78.0) vs. 67 (64.0–70.0) vs. 60 (55.0–63.0) vs. 53.0 (50.0–56.0) ($p<0.0001$); and 56.0 (55.0-59.3) vs. 56.0 (51.8–58.3) vs. 50.5 (45.0-53.3) vs. 45.5 (43.0-50.3) ($p<0.0001$), respectively. The pairwise comparisons revealed that the BIS values of patients in Group D2 and Group D3 were significantly different from those of patients in Group C ($P<0.017$), while those of patients in Group D1 were not significantly different from those of patients in Group C ($P>0.017$). This finding indicates that 0.5 μg kg^{-1} or 0.75 μg kg^{-1} dexmedetomidine preoperatively can help reach the target depth of anesthesia in children more quickly during inhalation

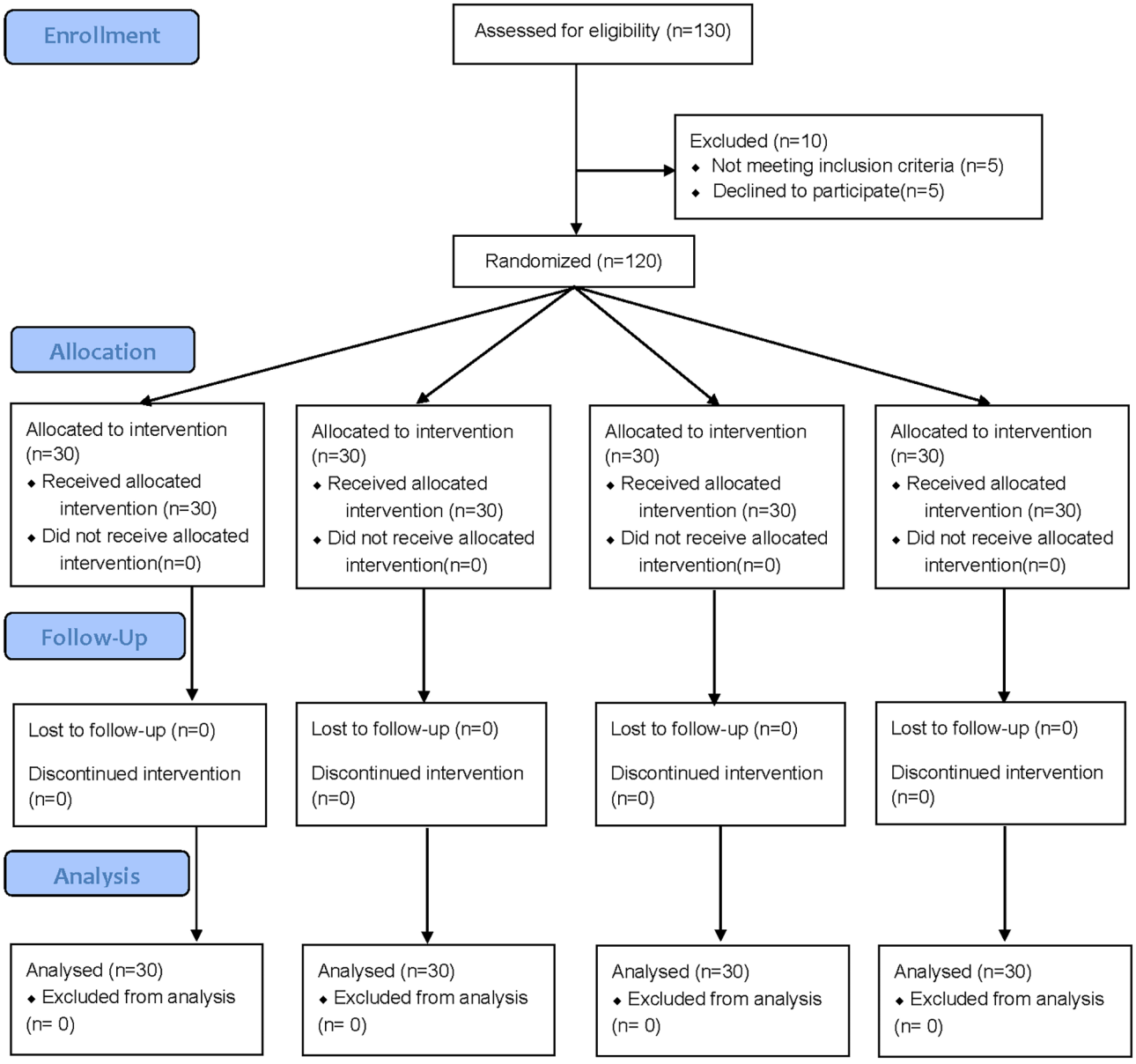

Fig. 1 Study flow chart

Table 1 Patient characteristic data and surgical characteristics of children. Values are mean (standard deviation) unless otherwise stated. Group C, preoperative administration with saline; Group D1, preoperative administration with 0.25ug kg^{-1} dexmedetomidine; Group D2, preoperative administration with 0.5ug kg^{-1} dexmedetomidine; Group D3, preoperative administration with 0.75ug kg^{-1} dexmedetomidine

	Group C($n=30$)	Group D1($n=30$)	Group D2($n=30$)	Group D3($n=30$)
Age(yr)	7.4(1.6)	8.3(1.9)	7.6(1.7)	7.8(1.9)
Weight(kg)	25.8(5.7)	30.4(9.0)	27.0(8.2)	27.7(7.7)
Gender(M/F)	11/9	10/10	11/9	13/7
Height (cm)	125.3(14.2)	128.5(15.5)	126.4(11.2)	127.5(13.2)
Operation time(min)	61.0(12.2)	67.0(23.2)	66.7(14.0)	69.7(17.4)

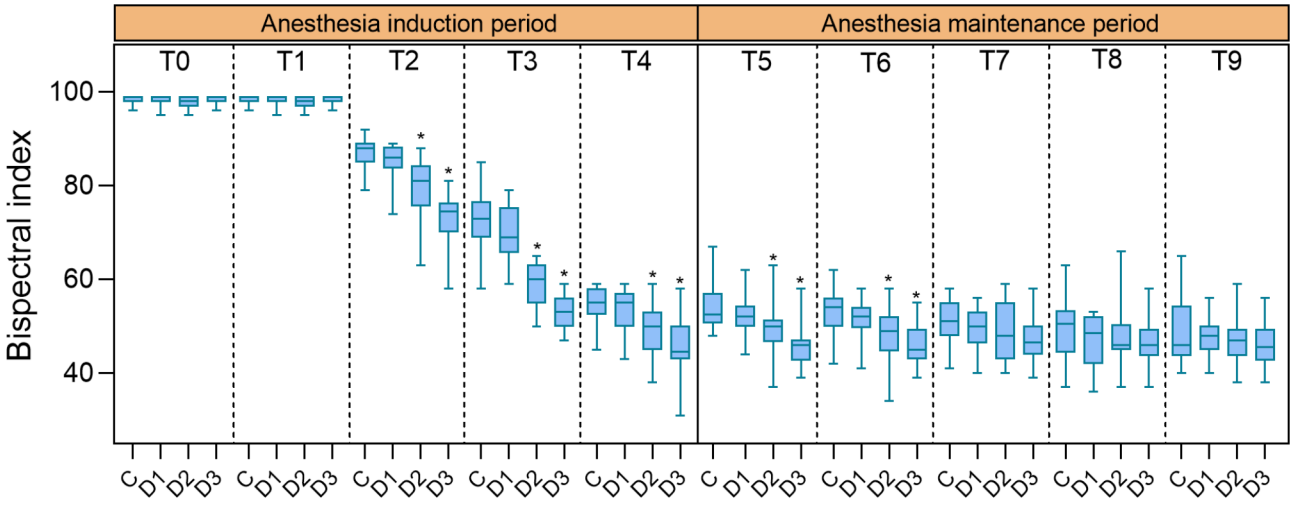

Fig. 2 Box plot of BIS values by study groups across different study times: T0, before dexmedetomidine administration; T1, after dexmedetomidine administration; T2, end-tidal sevoflurane concentration (ETsevo) 1%; T3, ETsevo 2%; T4, ETsevo 3%; T5, surgical incision; T6, 15 min(min) after surgical incision; T7, 30 min after surgical incision; T8, 45 min after surgical incision; T9, 60 min after surgical incision. * $P<0.017$ vs. Group C after Mann-Whitney U-test. Group C, preoperative administration with saline; Group D1, preoperative administration with 0.25ug kg^{-1} dexmedetomidine; Group D2, preoperative administration with 0.5ug kg^{-1} dexmedetomidine; Group D3, preoperative administration with 0.75ug kg^{-1} dexmedetomidine

induction with sevoflurane. During the maintenance of anesthesia, children pretreated with dexmedetomidine still had lower BIS values during the first 15 min than did those in the control group. The median BIS values of patients in Group C, Group D1, Group D2 and Group D3 at T5 and T6 were as follows: 52.5 (50.8–57.0) vs. 52.0 (50.0-54.3) vs. 50.0 (46.8–51.3) vs. 46.0 (42.8–47.0) ($p<0.0001$); and 54.0 (50.0–56.0) vs. 52.0 (49.8–54.0) vs. 49.0 (44.8–52) vs. 45.0 (43.0-49.3) ($p<0.0001$), respectively. Similarly, pairwise comparisons revealed that the BIS values of patients in Group D2 and Group D3 were significantly different from those of patients in Group C ($P<0.017$), while those of patients in Group D1 were not significantly different from those of patients in Group C ($P>0.017$).

Table 2 shows the end-tidal sevoflurane (ETsevo) concentrations in each group during the maintenance period of anesthesia. During anesthesia maintenance, children pretreated with dexmedetomidine had lower ETsevo concentrations than did those in the control group. The median ETsevo concentrations of patients in Group C, Group D1, Group D2 and Group D3 at T6, T7 and T8 were 3.0 (2.8–3.1) vs. 2.8 (2.5-3.0) vs. 2.6 (2.3–2.7) vs. 2.4 (2.1–2.7), $p<0.0001$; 3.0 (2.9–3.2) vs. 2.8 (2.5-3.0) vs. 2.5 (2.2–2.9) vs. 2.1 (2.0-2.5), $p<0.0001$; 3.0 (2.8-3.0) vs. 2.8 (2.4–3.2) vs. 2.6 (2.4-3.0) vs. 2.5 (2.3–2.8), $p=0.001$. The pairwise comparisons revealed that the BIS values of patients in Group D2 and Group D3 were significantly different from those in Group C ($P<0.017$), while those in Group D1 were not significantly different from those in Group C ($P>0.017$). This indicates that children pretreated with 0.5 μg kg^{-1} or 0.75 μg kg^{-1} dexmedetomidine required less sevoflurane to maintain the target depth of anesthesia.

Table 2 also shows the other perioperative data of the patients in each group. Children pretreated with dexmedetomidine have a lower intraoperative heart rate. The mean intraoperative heart rates of Group C, Group D1, Group D2 and Group D3 were 92.2 (9.5), 85.9 (8.9), 81.2 (9.1) and 76.3 (11.0), respectively ($p<0.0001$). Similarly, children pretreated with dexmedetomidine have a lower intraoperative mean arterial pressure. The mean intraoperative arterial pressures of Group C, Group D1, Group D2 and Group D3 were 61.8 (7.9), 59.2 (6.7), 58.1 (9.5)

Table 2 Secondary outcome data. Values are median (inter-quartile range) or mean (standard deviation) for continuous variables and number of patients (%) for categorical variables

	Group C($n=30$)	Group D1($n=30$)	Group D2($n=30$)	Group D3($n=30$)	*P* value
ETsevo					
T5	3.0(2.8–3.1)	2.9(2.7–3.1)	2.7(2.6–3.1)	2.9(2.5-3.0)	0.083[a]
T6	3.0(2.8–3.1)	2.8(2.5-3.0)	2.6(2.3–2.7)*	2.4(2.1–2.7)*	< 0.0001 [a]
T7	3.0(2.9–3.2)	2.9(2.5-3.0)	2.5(2.2–2.9)*	2.1(2.0-2.5)*	< 0.0001 [a]
T8	3.0(2.8-3.0)	2.8(2.4–3.2)	2.6(2.4-3.0)*	2.5(2.3–2.8)*	0.001 [a]
T9	2.9(2.6–3.1)	2.8(2.5-3.0)	2.7(2.4-3.0)	2.5(2.2-3.0)	0.134 [a]
Heart rate (min^{-1})	92.2(9.5)	85.9(8.9)#	81.2(9.1)#	76.3(11.0)#	< 0.0001[b]
Bradycardia (n, %)	2(6.7)	3(10.0)	4(13.3)	5(16.7)	0.779[c]
Mean arterial pressure (mm Hg)	61.8(7.9)	59.2(6.7)	58.1(9.5)	53.2(8.6)#	0.001 [b]
Hypotension (n, %)	0(0)	1(3.3)	1(3.3)	2(6.7)	0.901[c]
Emergence time (min)	32.1(4.4)	32.9(4.2)	33.4(4.5)	34.9(6.5)	0.175[b]
Time in PACU (min)	22.8(6.8)	23.5(6.8)	25.3(6.9)	26.1(6.9)	0.207[b]
Delayed emergence (n, %)	0(0)	0(0)	0(0)	1(3.3)	1.000[c]
Intraoperative awareness (n, %)	0(0)	0(0)	0(0)	0(0)	-

[a]Kruskal-Wallis test

[b]One-way ANOVA

[c]Chi-square test

*$P < 0.017$ vs. Group C after Mann-Whitney U-test

#$P < 0.05$ vs. Group C after Tukey Post Hoc Test

T5, surgical incision; T6, 15 min(min) after surgical incision; T7, 30 min after surgical incision; T8, 45 min after surgical incision; T9, 60 min after surgical incision. Group C, preoperative administration with saline; Group D1, preoperative administration with 0.25ug kg^{-1} dexmedetomidine; Group D2, preoperative administration with 0.5ug kg^{-1} dexmedetomidine; Group D3, preoperative administration with 0.75ug kg^{-1} dexmedetomidine. ETsevo, end-tidal sevoflurane concentration; PACU, post anaesthesia care unit

and 53.2 (8.6), respectively ($p=0.001$). Remarkably, the incidence of intraoperative bradycardia or hypotension was similar among the groups. In addition, the PACU discharge time and incidence of delayed emergence were similar among the groups. No intraoperative awareness was found in any of the four groups.

Discussion

This prospective randomized study demonstrated that children who received 0.5 μg kg^{-1} or 0.75 μg kg^{-1} dexmedetomidine preoperatively were more likely to achieve the target depth of anesthesia (BIS less than 60) during anesthesia induction and had lower BIS values during the early stage of anesthesia maintenance. Furthermore, premedication with 0.5 μg kg^{-1} or 0.75 μg kg^{-1} dexmedetomidine reduced the requirement for sevoflurane in children during general anesthesia.

Dexmedetomidine is widely used for pediatric anesthesia and has many benefits, including relieving perioperative anxiety and reducing postoperative delirium [11, 14]. Unlike opioids dexmedetomidine does not impair ventilation and therefore does not slow down inhalational induction. Nevertheless, few studies have focused on the effect of dexmedetomidine on the depth of anesthesia in children. Prospective, randomized, multicenter studies suggest that there may be a correlation between the depth of anesthesia and long-term postoperative mortality [15]. In this study, premedication with dexmedetomidine had an obvious synergistic effect on sevoflurane inhalation anesthesia in children, as indicated by a dose-dependent decrease in the BIS value during anesthesia induction and the early stage of anesthesia maintenance. This finding is similar to the findings of a previous study in adults [10]. It has been suggested that dexmedetomidine augments the effect of sevoflurane anesthesia, probably by regulating thalamo-cortical networks, which enhances sevoflurane anesthesia and may be associated with decreased thalamocortical connectivity [16]. Moreover, other studies have shown that the synergistic anesthetic effect of dexmedetomidine may be related to its action on α2 receptors in the cerebral central nervous system [17, 18]. Hemodynamic inhibition by dexmedetomidine can lead to decreased cerebral perfusion and cerebral metabolism, which may also be one of the reasons why dexmedetomidine reduces the BIS value [19].

Sevoflurane is currently the most widely used inhalation anesthetic for pediatric clinical anesthesia induction and intraoperative maintenance and has obvious advantages. The correlation between the BIS and sevoflurane inhalation is good, and the use of the BIS to monitor the depth of sevoflurane anesthesia is reliable [20]. There was no significant difference between Group D1 and Group C, indicating that preoperative infusion of a small dose (0.25 μg/kg/h) of dexmedetomidine did not reduce the dosage of sevoflurane used during the operation. Our results showed that premedication with 0.5 μg/kg and 0.75 μg/kg dexmedetomidine significantly reduced the requirement for sevoflurane during the

anesthesia maintenance phase, which may be related to its spinal cord-level analgesia [21]. Hayashi K et al. [22] suggested that the use of dexmedetomidine as a sedative and anesthetic adjuvant during the perioperative period could reduce the dosage of sevoflurane used and the incidence of postoperative neurological complications, and the combination of dexmedetomidine and sevoflurane had synergistic or enhancing effects on EEG activity. Numerous studies have shown that dexmedetomidine can significantly reduce the amount of sevoflurane used during general anesthesia [10, 23, 24]. It is worth noting that these studies are limited to adults, and there is a lack of data on children. Hence, this study provides data supporting the management of sevoflurane combined with dexmedetomidine anesthesia in children.

Hypotension and bradycardia are common adverse reactions to dexmedetomidine [25, 26]. Our data showed that children treated with different doses of dexmedetomidine preoperatively also showed different degrees of decreases in heart rate and mean arterial pressure during surgery compared with those in the control group. Nevertheless, there was no significant difference in the incidence of hypotension or bradycardia among the four groups. This suggested that the preoperative administration of 0.75 μg kg^{-1} dexmedetomidine is relatively safe for perioperative haemodynamics in children. However, the sample size of this study was not estimated based on bradycardia or hypotension outcomes, so the sample size of this study may be insufficient for such outcomes. Dexmedetomidine has a half-life of 120 min [27], and a retrospective study of pediatric patients found evidence for a small association of intraoperative dexmedetomidine with the duration of recovery, with a potential dose relationship equivalent to an approximately 15-minute delay per μg kg^{-1} of dexmedetomidine administered [28]. Notably, in this study, there was no significant difference in emergence time or PACU discharge time among the four groups, and only one case of delayed emergence was reported in a child who received 0.75 μg kg^{-1} of dexmedetomidine preoperatively. The reason may be that the time point at which dexmedetomidine was administered in this study was before the induction of anesthesia, and dexmedetomidine was not continuously pumped during the operation.

Overall, this study showed that preoperative dexmedetomidine administration significantly reduced sevoflurane use during general anesthesia in children without significant hypotension, bradycardia or postoperative delayed emergence. Recent studies have shown that multiple inhalation exposures to sevoflurane may cause neurotoxicity in children [29]. The neuroprotective effects of dexmedetomidine and its ability to reduce the dose of sevoflurane used during general anesthesia make it particularly suitable for children who require repeated anesthesia [29]. Moreover, preoperative dexmedetomidine administration was associated with reduced incidence of perioperative respiratory adverse events [30]. Hence, preoperative dexmedetomidine administration can be widely used in children as an adjunct to general anesthesia.

There are a few limitations in this study. First, the study was a single-center study, which limits the generalizability of the results of this study. Second, the sample size of the study was relatively small, which may be underpowered for data analysis of some secondary outcomes. Third, although each subject underwent caudal block, we were unable to fully exclude the influence of pain on the sevoflurane dose used. Finally, caudal block may have influenced the outcome of this study. Caudal block has been shown to reduce BIS values in children under sevoflurane inhalation anesthesia [31]. In this study, although all groups of children underwent caudal block, there was no effective way to control or assess its biased effect on the outcome of BIS values.

Conclusions

In conclusion, intravenous premedication with 0.5 μg kg^{-1} or 0.75 μg kg^{-1} dexmedetomidine had a significant synergistic effect on sevoflurane inhalation anesthesia in children, which was reflected in the rapid attainment of the target depth of anesthesia in the induction period and the lower BIS value during the early stage of anesthesia maintenance. Notably, in this study, premedication with dexmedetomidine did not increase the incidence of perioperative hypotension or bradycardia or prolong the time to recovery from anesthesia. This study provides new and available data for the use of dexmedetomidine in pediatric anesthesia management.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12871-025-02946-x.

Supplementary Material 1

Acknowledgements

The authors thank all anaesthesiologists, urologic surgeons and nurses who contributed to the study.

Author contributions

ZX and LW contributed to the conception, design, data collection, analysis, interpretation, and writing throughout the entire study process. SWW contributed to data collection, analysis, and interpretation. EYY and ZC contributed to data collection and interpretation. ZD contributed to the conception, design, analysis, interpretation, and manuscript revision.

Funding

This work was supported by Natural Science Foundation of Hunan Province (No. 2019JJ50294).

Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The research protocol for this project has been meticulously designed, incorporating a detailed and comprehensive informed consent form that thoroughly safeguards the rights and well-being of the participants, adhering to the principles outlined in the Helsinki Declaration. After careful review by the ethics committee, the project has received approval to proceed. The reviewing ethics committee is based at the Affiliated Children's Hospital of Xiangya School of Medicine, Central South University (also known as the Hunan Children's Hospital); the ethical approval number assigned is HCHLL-2019-10.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

CONSORT statement
Our study conformed to the CONSORT guidelines.

Received: 21 November 2024 / Accepted: 4 February 2025
Published online: 14 February 2025

References

1. Myles PS, Leslie K, McNeil J, Forbes A, Chan MT. Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial. Lancet. 2004;363:1757–63.
2. Laferrière-Langlois P, Morisson L, Jeffries S, Duclos C, Espitalier F, Richebé P. Depth of Anesthesia and Nociception Monitoring: current state and vision for 2050. Anesth Analg. 2024;138:295–307.
3. Frelich M, Lečbychová K, Vodička V, et al. Effect of BIS-guided anesthesia on emergence delirium following general anesthesia in children: a prospective randomized controlled trial. Anaesth Crit Care Pain Med. 2024;43:101318.
4. Lamperti M, Romero CS, Guarracino F, et al. Preoperative assessment of adults undergoing elective noncardiac surgery: updated guidelines from the European Society of Anaesthesiology and Intensive Care. Eur J Anaesthesiol. 2025;42:1–35.
5. Glass Peter S, Bloom M, Kearse L, Rosow C, Sebel P, Manberg P. Bispectral analysis measures sedation and memory effects of propofol, midazolam, isoflurane, and alfentanil in healthy volunteers. Anesthesiology. 1997;86:836–47.
6. Liu PP, Wu C, Wu JZ, et al. The prediction probabilities for emergence from sevoflurane anesthesia in children: a comparison of the perfusion index and the bispectral index. Paediatr Anaesth. 2018;28:281–6.
7. Chambers NA, Pascoe E, Kaplanian S, Forsyth I. Ingestion of stimulant medications does not alter bispectral index or clinical depth of anesthesia at 1 MAC sevoflurane in children. Paediatr Anaesth. 2012;22:341–4.
8. Doze VA, Chen BX, Maze M. Dexmedetomidine produces a hypnotic-anesthetic action in rats via activation of central alpha-2 adrenoceptors. Anesthesiology. 1989;71:75–9.
9. Hendrickx JF, Eger EI 2nd, Sonner JM, Shafer SL. Is synergy the rule? A review of anesthetic interactions producing hypnosis and immobility. Anesth Analg. 2008;107:494–506.
10. Mizrak A, Ganidagli S, Cengiz MT, Oner U, Saricicek V. The effects of DEX premedication on volatile induction of mask anesthesia (VIMA) and sevoflurane requirements. J Clin Monit Comput. 2013;27:329–34.
11. Du Z, Zhang XY, Qu SQ, et al. The comparison of dexmedetomidine and midazolam premedication on postoperative anxiety in children for hernia repair surgery: a randomized controlled trial. Paediatr Anaesth. 2019;29:843–9.
12. Du Z, Wei SW, Zhang XY, Xiang Z, Qu SQ. The effect of dexmedetomidine premedication on postoperative systemic inflammatory response in children undergoing hernia repair surgery: a randomized controlled trial. Paediatr Anaesth. 2021;31:794–801.
13. Akhondzadeh R, Olapour A, Rashidi M, Elyasinia F. Comparison of Sedation withDexmedetomidine Alfentanil Versus ketamine-alfentanil in patients undergoing closed reduction of nasal fractures. Anesth Pain Med. 2020;10:e102946.
14. Shi M, Miao S, Gu T, Wang D, Zhang H, Liu J. Dexmedetomidine for the prevention of emergence delirium and postoperative behavioral changes in pediatric patients with sevoflurane anesthesia: a double-blind, randomized trial. Drug Des Devel Ther. 2019;13:897–905.
15. LeslieK,Myles Ps,Forbes A, et al. The effect of bispectral index monitoring on long-term survival in the B-aware trial. Anesth Analg. 2010;110:816–22.
16. Zhang L, Li H, Deng L, et al. Electroencephalogram mechanism of Dexmedetomidine Deepening Sevoflurane Anesthesia. Front Neurosci. 2022;16:913042.
17. Weber F, Walhout LC, Escher JC. The impact of Narcotrend™ EEG-guided propofol administration on the speed of recovery from pediatric procedural sedation-A randomized controlled trial. Paediatr Anaesth. 2018;28:443–9.
18. Wang C, Yuan W, Hu A, et al. Dexmedetomidine alleviated sepsis–induced myocardial ferroptosis and septic heart injury. Mol Med Rep. 2020;22:175–84.
19. Dutta A, Sethi N, Sood J, et al. The Effect of Dexmedetomidine on Propofol requirements during Anesthesia administered by Bispectral Index-guided closed-Loop Anesthesia Delivery System: a randomized controlled study. Anesth Analg. 2019;129:84–91.
20. Walkden GJ, Pickering AE, Gill H. Assessing long-term neurodevelopmental outcome following General Anesthesia in Early Childhood: challenges and opportunities. Anesth Analg. 2019;128:681–94.
21. Meinberg AC, Joã, Meinberg OPR, et al. Effect of Dexmedetomidine and remifentanil on renal function in patients undergoing bariatric surgery. Open J Anesthesiology. 2020;10:120–33.
22. Hayashi K, Sawa T, Matsuura M. Anesthesia depth-dependent features of electroencephalographic bicoherence spectrum during sevoflurane anesthesia. Anesthesiology. 2008;108:841–50.
23. Yoo JY, Kwak HJ, Kim YB, et al. The effect of dexmedetomidine pretreatment on the median effective bolus dose of propofol for facilitating laryngeal mask airway insertion. J Anesth. 2017;31:11–7.
24. Gerresheim G, Schwemmer U. Dexmedetomidin [Dexmedetomidine] Anaesthesist. 2013;62:661–74.
25. Okello MO, Mung'ayi V, Adam R, Kabugi J. A comparison of risk of hypotension using standard doses of remifentanil versus dexmedetomidine infusions in adult patients undergoing surgery under general anaesthesia at the Aga Khan University Hospital, Nairobi. Afr Health Sci. 2018;18:1267–82.
26. Amer AM, Youssef AM, El-Ozairy HS, El-Hennawy AM. Propofol-cetamina versus dexmedetomidina-cetamina para sedação durante endoscopia digestiva alta em pacientes pediátricos: estudo clínico randomizado [Propofol-ketamine versus dexmedetomidine-ketamine for sedation during upper gastrointestinal endoscopy in pediatric patients: a randomized clinical trial]. Braz J Anesthesiol. 2020;70:620–6.
27. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: a novel sedative-analgesic agent. Proc (Bayl Univ Med Cent). 2001;14:13–21.
28. West N, Görges M, Poznikoff A, Whyte S, Malherbe S. Association of dexmedetomidine with recovery room and hospital discharge times: a retrospective cohort analysis. Paediatr Anaesth. 2021;31:1170–8.
29. Andropoulos DB. Neuroprotective strategies in anesthesia-induced neurotoxicity. Best Pract Res Clin Anaesthesiol. 2023;37(1):52–62.
30. Shen F, Zhang Q, Xu Y, et al. Effect of Intranasal Dexmedetomidine or Midazolam for Premedication on the occurrence of respiratory adverse events in children undergoing Tonsillectomy and Adenoidectomy: a Randomized Clinical Trial. JAMA Netw Open. 2022;5(8):e2225473.
31. Davidson AJ, Ironfield CM, Skinner AV, Frawley GP. The effects of caudal local anesthesia blockade on the Bispectral Index during general anesthesia in children. Paediatr Anaesth. 2006;16(8):828–33.

Publisher's note