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Impact of dexmedetomidine on agitation and inflammatory response during recovery from anesthesia in young children following cochlear implantation surgery

Qing Cheng[1†], Chao-Yang Chen[1†], Xiang Li[1], Li-Jun Wu[1] and Ze-Yu Zhao[1*]

Abstract

Objective To evaluate the impact of dexmedetomidine (Dex) on agitation and inflammatory response during recovery from anesthesia in young children following cochlear implantation surgery.

Methods We randomly divided 80 children who underwent unilateral cochlear implantation into two equal groups. Group D received an intravenous infusion of Dex after induction of anesthesia, while those in group C received an equal volume of saline infusion. The mean arterial pressure (MAP) and heart rate (HR) of children in the two groups were recorded at four different time intervals: before induction of anesthesia (T_0); 30 min after intravenous infusion of Dex (T_1); upon admission to the post-anesthesia care unit (PACU) (T_2); and at the time of being transferred out of the PACU (T_3). At T3, we also recorded general information.

Results The MAP and HR in group D showed more consistent trends during the anesthesia recovery period when compared to those in group C. Children in group D had a significantly lower crying, requires increased O_2 administration, increased vital signs, expression and sleepless score (CRIES score), pediatric anesthesia emergence delirium (PAED) score, and incidence of agitation than in group C ($P<0.01$). The rate of supplementary pain relief for the children was lower in group D than in group C ($P<0.01$). At T_3, serum levels of interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) were lower in children in group D than in group C ($P<0.01$). Compared to T_0, the levels of serum IL-6 and TNF-α were higher in both groups at T_3 ($P<0.01$).

Conclusion We found that the use of Dex helped reduce the occurrence and severity of agitation during anesthesia recovery in children after cochlear implantation surgery and improved postoperative inflammatory reactions.

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Keywords Anesthesia recovery, Children, Cochlear implantation, Dexmedetomidine, Inflammation, Psychomotor agitation, Young age

Introduction

Profound binaural deafness is defined as hearing loss in the range of 1 kHz and higher frequencies, with hearing thresholds above 90 dB [1]. Cochlear implantation is a common treatment, and the best time for implantation depends on the age of the onset of deafness [2]. For pre-speech deafness, the ideal window for implantation ranges from 12 months to six years of age [3], with children typically being operated on at the age of about 2 years in order to keep up with postoperative language function training and normal school-age education [4].

Pediatric patients, particularly those of very young age, exhibit significant physiological and psychological differences compared to surgical patients of other age groups. For instance, the organ systems in young children are not fully developed, which affects their metabolism and tolerance of anesthetic agents. Additionally, these patients are often unable to communicate their discomfort effectively during the recovery from anesthesia, unlike older children or adults, which complicates anesthetic management. Given that surgical procedures in this population often occur near critical neural and vascular structures, there is a heightened demand for precision and safety in anesthesia administration. Furthermore, to minimize the psychological and physiological stress response of the child during surgery, it is imperative to select appropriate anesthetic drugs and techniques to ensure patient comfort and safety. Consequently, cochlear implantation presents unique challenges in anesthetic management, necessitating further research to optimize anesthetic protocols for this patient population [5].

Pharmacological interventions are often necessary to reduce agitation in children and safely navigate the post-anesthesia recovery period. Dexmedetomidine (Dex) is a highly selective α-adrenergic agonist with dose-dependent analgesic, sedative, anti-inflammatory, and anxiolytic effects without significant respiratory depression [6]. It has been extensively used in children during the perioperative recovery period to reduce the occurrence of agitation [7–9]. However, further study is needed to determine the impact of Dex on agitation and inflammatory response during the anesthesia recovery period in young children undergoing cochlear implantation.

Therefore, in this study, our primary objective was to assess the impact of Dex on agitation and inflammatory response during the anesthesia recovery phase in younger children undergoing cochlear implantation. Our aim was also to establish a theoretical foundation for the use of anesthesia in this demographic and to offer technical assistance for addressing the rehabilitation of hearing impairment during the surgical phase.

Materials and methods

General information

This study was approved by the Medical Ethics Committee of our hospital, and we obtained informed consent from the guardians of the children included in the study (Ethics Approval No. CKLL2023004). From October 2022 to September 2023, a total of 87 children who underwent unilateral cochlear implantation surgery at Sichuan Bayi Rehabilitation Center were assessed for eligibility. Inclusion criteria: (1) patients undergoing elective general anesthesia surgery with a surgery duration > 1 h and ≤ 3 h; (2) aged ≥ 9 months and ≤ 3 years; (3) any gender, body weight of ≥ 8 kg; and (4) health status of grade I or II as per the American Society of Anesthesiologists (ASA) classification. To be excluded sinus bradycardia or atrioventricular block ($n = 3$), a history of respiratory tract infection within 2 weeks before surgery ($n = 1$), severe laryngospasm and bronchospasm during anesthesia ($n = 1$), laryngeal cartilage dysplasia ($n = 1$), coexisting congenital heart disease and NYHA cardiac function classification ≥ grade II ($n = 1$). Finally, 80 cases were included in this study. We randomly assigned the children to two groups: the Dex group (Group D) and the control group (Group C), with 40 cases in each group. Since designer determined the groups, the anesthesia nurse prepared medication according to the grouping method, and neither the subjects nor the anesthesiologist knew the treatment allocation (Fig. 1).

Anesthesia methods

Preoperatively, the child was fasted for 6 h without solid foods and 2 h without liquids. The child was administered intravenous injections of midazolam at a dosage of 0.1 mg/kg and penehyclidine at a dosage of 0.01 mg/kg in the anesthesia preparation room. Blood pressure, electrocardiogram, pulse oximetry (SPO_2), and partial pressure of end-expiratory carbon dioxide ($P_{ET}CO_2$) were routinely monitored during surgery.

Medications for inducing anesthesia: sufentanil 0.3 μg/kg, atracurium besylate 0.2 mg/kg, and propofol 1.5–2 mg/kg. Mechanical ventilation was initiated following tracheal intubation. Respiratory parameters: pressure-controlled ventilation (PCV) mode, inspiratory pressure 10–15 cmH_2O (1 $cmH_2O = 0.098$ kilopascal), respiratory rate 16–22 breaths/min, inspiratory to expiratory ratio of 1:2, oxygen flow rate 2 L/min, and $P_{ET}CO_2$ maintained at 35–45 mmHg (1 mmHg = 0.133 kPa).

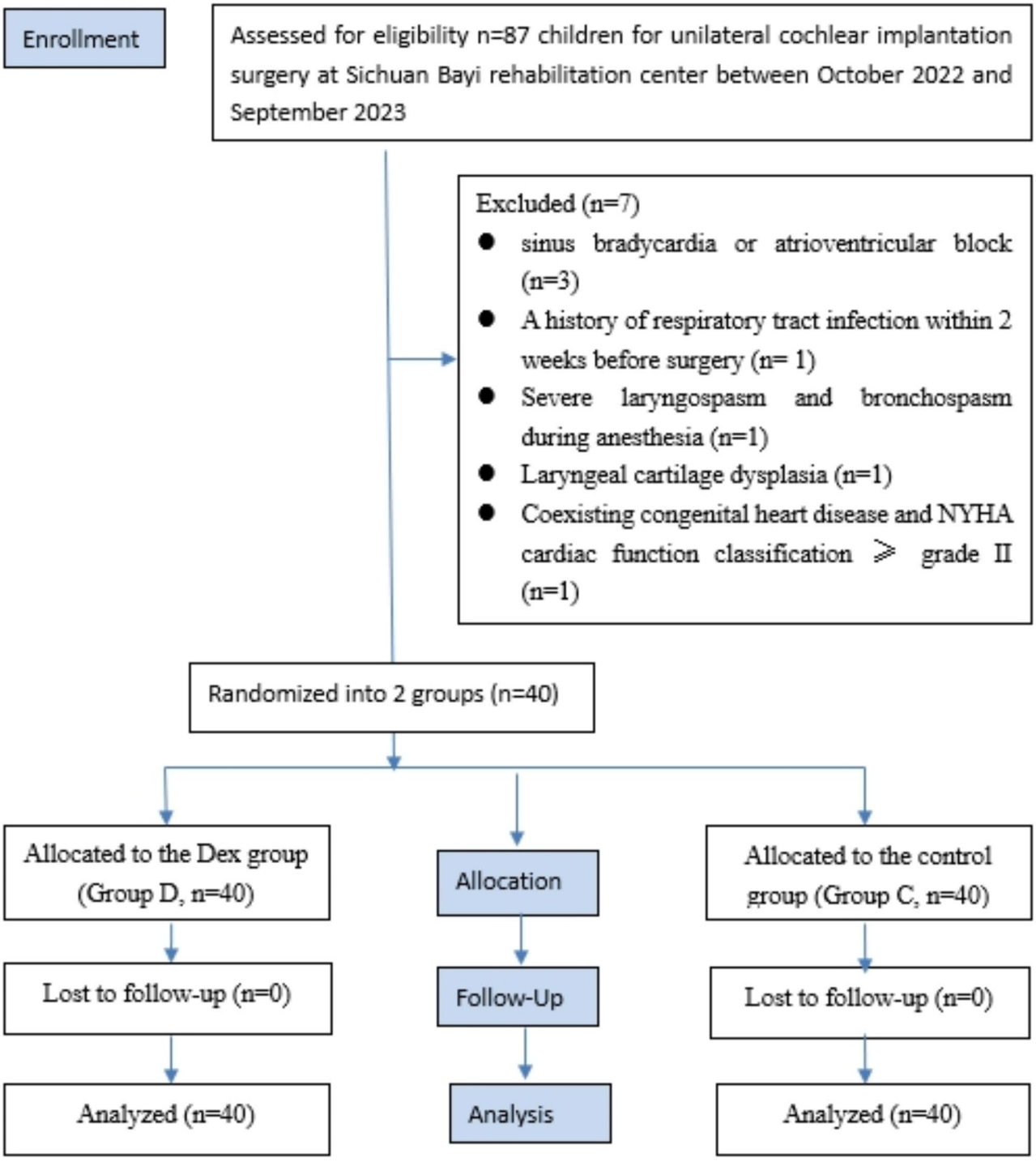

Fig. 1 CONSORT diagram

Anesthesia maintenance: intravenous infusion of remifentanil 0.15–0.2 μg/(kg- min) and inhalation of sevoflurane 2–3% for maintenance.

In group D, following anesthesia induction, intravenous infusion of Dex was administered (Yangtze River Pharmaceutical (Group) Co., Ltd., batch number: 22071631, 20 mL: (0.2 mg) 0.5 μg/(kg-h). Children in group C received an infusion of an equal volume of saline. Dex was stopped 30 min before the end of the surgery, while remifentanil and sevoflurane were stopped at the end of the surgery. Sufentanil was injected intravenously at a dose of 1 μg. The tracheal catheter was removed when

spontaneous respiration was ≥ 14 breaths/min and tidal volume (VT) ≥ 8 ml/kg.

The patient was then transferred to the post anesthesia care unit (PACU). Nasal catheter oxygen was administered at a rate of 2 L/min, and electrocardiogram(ECG), blood pressure, SpO_2, and respiration were continuously monitored. During the anesthesia recovery period, if the pain score was ≥ 4, intravenous sufentanil 0.1 μg/kg was administered for additional pain relief.

Observation indexes

The mean arterial pressure (MAP) and heart rate (HR) of the two groups were recorded at specific time intervals: before induction of anesthesia (T_0), 30 min after intravenous infusion of Dex (T_1), upon admission to the PACU (T_2), and at the time of transfer out of the PACU (T_3). We recorded the duration of anesthesia, surgery, extubation time (time from discontinuation of anesthesia medication to extubation), and awakening time (time from discontinuation of anesthesia medication to awakening) for children in both groups, as well as pain scores and the incidence of agitation at the time of transfer out of the PACU.

We assessed pain using the five-item CRIES score: crying (C); requires increased oxygen administration (R); changes in vital signs (I); changes in facial expression (E); and sleeplessness (S) [10]. The scoring index is shown in Table 1.

We used the pediatric anesthesia emergence delirium scale (PAED), developed by Sikich et al., for evaluating the level of agitation. The PAED items were as follows: The child follows instructions and is communicative; the child's behavior is purposeful; the child is aware of the surroundings; the child is not withdrawn; and the child cries and cannot be comforted. Each item was graded using a 5-point rating scale [11]. For the first three items, the grades were: none (4 points); poor (3 points); good (2 points); very good (1 point); and excellent (0 points). For the last 2 items, the grades were: very severe (4 points); severe (3 points); moderate (2 points); mild (1 point); and none (0 points). The scores for each item were added, and a total score of ≥ 12 was defined as agitation.

Table 1 CRIES Rating Scale

Item	0 point	1 point	2 points
Crying	None	Loud, high pitched voice	Cannot be comforted easily
Maintaining $SPO_2 > 95\%$ Whether oxygen is needed	No	Oxygen concentration < 30%	Oxygen concentration > 30%
Vital signs	HR and BP maintained at preoperative levels	HR and BP increased < 20% from preoperative levels	HR and BP increase > 20% from preoperative levels
Expression	Nothing unusual	Painful expression	Very painful expression, moaning
Insomnia	None	Often awake	Always awake

Note: HR, heart rate; BP, blood pressure

We also documented the incidence of respiratory depression (respiratory rate < 12 breaths/min), sinus bradycardia (heart rate < 60 beats/min), and the need for supplementary pain relief during the recovery from anesthesia. Two mL of venous blood was drawn at T_0 and T_3, and interleukin-6 (IL-6) and tumor necrosis factor α (TNF-α) were detected using enzyme immunoassay.

Statistical analysis

The sample size was calculated using pass 11.0 software. In a study by Tsiotou AG, the incidence of emergence agitation in children under general anesthesia was 41.4% [12]. We expect the incidence of agitation with Dex to be reduced to 18%, so the rate in group D was 0.18, and the rate in group C was 0.41. The superiority test of the two groups' independent sample rate was used, $\alpha = 0.025, \beta = 0.2$, The sample size ratio of the two groups was 1:1. The sample size was 40, so 40 cases in each group were selected for the study.

We used SPSS 25.0 statistical software for processing the data in this study. Non-normally distributed quantitative data were represented as the median with quartile spacing [M(Q1, Q3)], while normally distributed quantitative data were represented as the mean ± standard deviation ($x \pm s$). Intra-group comparisons at different time points were conducted using the analysis of variance (ANOVA) with repeated measures design, and group comparisons were made using the paired *t*-test. U-test was used for the data that was not normally distributed. Counting information was expressed as cases (%), and the χ^2 test was used, with a *P* value of < 0.05 considered as indicating a statistically significant difference.

Results

There were no statistically significant differences when we compared the age, body weight, gender composition, ASA classification, surgical site, duration of anesthesia, duration of surgery, extubation time, and awakening time of the children in the two groups ($P > 0.05$, Table 2).

After testing for sphericity and correcting for degrees of freedom using the Greenhouse-Geisser method, we found that the two groups differed significantly in MAP and HR at various time intervals ($P < 0.05$). There was also a significant interaction between different time intervals and groups ($P < 0.05$). Furthermore, the differences in HR between the two groups were statistically significant across different time intervals ($P < 0.05$). Compared to group C, MAP and HR in group D decreased at T_1 -T_2 (T_1: $t = 2.047$, 2.422, T_2: $t = 2.280$, 3.239, $P < 0.05$ or < 0.01), and HR in group D decreased at T_3 ($t = 3.027$,

Table 2 Comparison of general information and surgical indicators between the two groups

Indicator	Group D ($n=40$)	Group C ($n=40$)	Statistical value	*P* value
Age [months, M(Q1,Q3)]	18(12,24)	22(14,28)	1.692	0.091
Weight (kg, $x \pm s$)	10.6 ± 1.5	10.1 ± 1.6	1.310	0.194
Gender (cases, male/female)	28/12	31/9	0.581	0.446
ASA classification (cases, I / II)	32/8	35/5	0.827	0.363
Surgical site (case, left/right)	4/36	6/34	0.346	0.556
Anesthesia duration (min, $x \pm s$)	132 ± 17	136 ± 12	1.409	0.163
Duration of surgery (min, $x \pm s$)	75 ± 16	79 ± 15	1.034	0.304
Extubation time (min, $x \pm s$)	6.4 ± 2.0	6.5 ± 1.6	0.123	0.902
Awakening time (min, $x \pm s$)	10.4 ± 2.6	9.0 ± 3.3	1.476	0.144

ASA, American Society of Anesthesiologists physical status

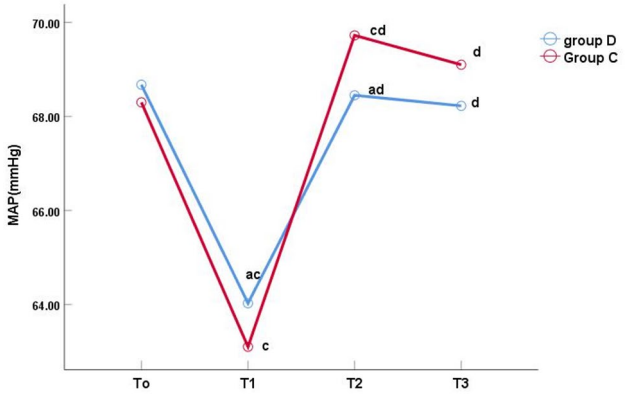

Fig. 2 Comparison of MAP at each time point between the two groups ($x \pm s$, $n=40$) Note: Compared with group C, $^{a}P<0.05$; compared with T_0, $^{c}P<0.01$; compared with T_1, $^{d}P<0.01$ MAP, mean arterial pressure; HR, heart rate

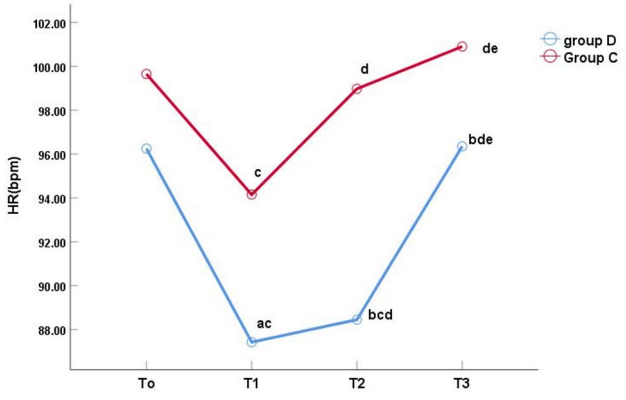

Fig. 3 Comparison of HR at each time point between the two groups ($x \pm s$, $n=40$) Note: Compared with group C, $^{a}P<0.05$, $^{b}P<0.01$; compared with T_0, $^{c}P<0.01$; compared with T_1, $^{d}P<0.01$; compared with T_2, $^{e}P<0.01$ MAP, mean arterial pressure; HR, heart rate

Table 3 Comparison of CRIES score, PAED score, and incidence of agitation between the two groups

Group	Number of cases	CRIES score (Median (Q1-Q3))	PAED score (points, $x \pm s$)	Incidence of agitation [cases (%)]
Group D	40	2(1–3)	9.1 + 1.6	4(10.00)
Group C	40	4(3–5)	12.1 + 2.6	23(57.50)
$t/\chi 2$ value		5.397	6.242	17.802
P value		< 0.001	< 0.001	< 0.001

Note: CRIES score, crying, requires increased O_2 administration, increased vital signs, expression and sleepless score; PAED score, pediatric anesthesia emergence delirium scale

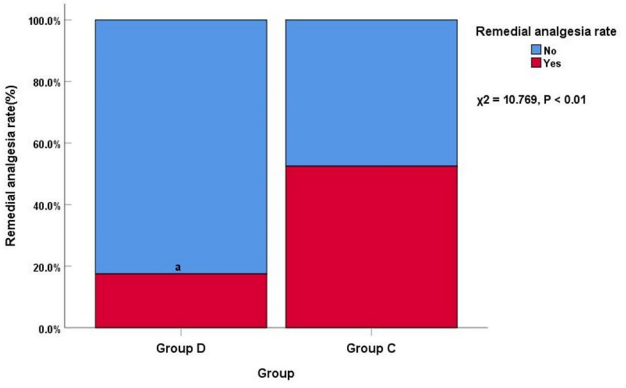

Fig. 4 Comparison of the rate of supplementary pain relief between the two groups Note: Compared with group C, $^{a}P<0.01$

$P<0.01$). Compared with T_0, MAP and HR in the two groups decreased at T_1 ($t=29.372$ and 7.902 in group D, 63.687 and 14.387 in group C, respectively, $P<0.01$). HR decreased at T_2 in group D ($t=3.853$, $P<0.01$); MAP was elevated at T_2 in group C ($t=10.679$, $P<0.01$). Compared with T_1, MAP and HR were higher at T_2 and T_3 in both groups; the t values were as follows: for group D, T_2: 20.348, 3.929; T_3: 11.491, 4.656; for group C, T_2: 42.801, 5.378; and T_3: 23.939, 5.915 ($P<0.01$). Compared with T_2, HR was higher at T_3 in group 2 ($t=3.211$, 2.990, $P<0.01$). The differences were not statistically significant ($P>0.05$) when we compared the remaining time intervals (Figs. 2 and 3).

Children in group D had a lower CRIES score, PAED score, and incidence of agitation when compared to those in group C. The difference was statistically significant ($P<0.01$, Table 3).

Respiratory depression and sinus bradycardia did not occur in either group during the anesthesia recovery period. The rate of supplementary pain relief was lower in group D (7/40 cases) compared to group C (21/40 cases) ($\chi^2=10.769$, $P<0.01$, Fig. 4).

Serum levels of IL-6 and TNF-α were lower in group D compared to group C at T_3 ($t=5.900$, 4.594, $P<0.01$). Compared with T_0, serum IL-6 and TNF-α levels were

Table 4 Comparison of IL-6 and TNF - α levels between two groups(pg/mL, $x \pm s$)

Group	Number of cases	IL-6		TNF-α	
		T_0	T_3	T_0	T_3
Group D	40	8.3 ± 5.2	14.0 ± 6.3[a b]	8.3 ± 3.6	16.7 ± 6.1 [a b]
Group C	40	8.1 ± 4.5	24.0 ± 8.7 [b]	9.7 ± 5.0	25 ± 59.7 [b]
t value		0.187	5.900	0.819	4.594
P value		0.852	0.000	0.415	0.000

Note: Compared with group C, [a]$P < 0.01$; Compared with T_0, [b]$P < 0.01$

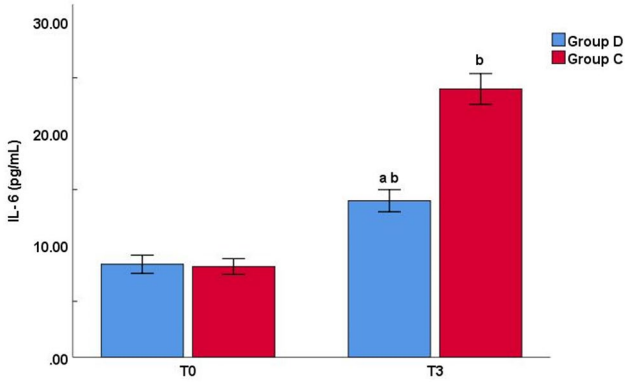

Fig. 5 Comparison of IL-6 levels between the two groups Note: Compared with group C, [a]$P < 0.01$; compared with T_0, [b]$P < 0.01$

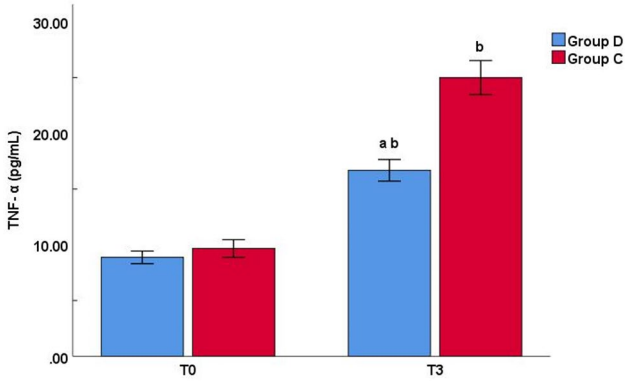

Fig. 6 Comparison of TNF-α levels between the two groups Note: Compared with group C, [a]$P < 0.01$; compared with T_0, [b]$P < 0.01$

elevated at T_3 in both groups (*t* values: group D: 9.848, 11.137; group C: 19.783, 15.477, respectively; $P < 0.01$; Table 4; Figs. 5 and 6, respectively).

Discussion

In this study, we selected Dex at a rate of 0.5 μg/(kg·h) for intravenous infusion based on literature references [13] and the findings documented in previous studies. Based on the pharmacokinetic characteristics of Dex [14], we prolonged its continuous infusion half-life (t1/2CS) by increasing the infusion time. The infusion was halted 30 min before the end of the surgery to time the child awakening promptly at the end of the surgery. Additionally, this timing strategy ensured that one of the elimination half-lives of Dex (2–3 h) covered the period of the child's resuscitation in the PACU.

Our results in this study demonstrated that Dex was effective in reducing the frequency and severity of agitation during the recovery from anesthesia in younger children undergoing cochlear implantation. Dex is a highly selective α_2-adrenoceptor agonist (α_2:α_1 = 1600:1). As an imidazole derivative, it inhibits the release of norepinephrine through the activation of G proteins located on the α_2-adrenoceptor within the blueprint nucleus of the central nervous system. This mechanism results in tonic suppression of the sympathetic nervous system [15] and activation of endogenous sleep-promoting pathways, leading to analgesia and sedation [16]. Dex maintains the patient in a stage III non-motorized eye sleep state, resembling a natural hypnosis-like process without inducing respiratory depression.

In prior investigations conducted by our team, it was demonstrated that Dex inhibits the onset of agitation by suppressing sympathetic activity, reducing the secretion of stress hormones, and attenuating the stress response [5, 9]. In line with these findings, in the current study, children in group D exhibited more consistent MAP and HR during the anesthesia recovery phase. Additionally, they had lower CRIES and PAED scores, a reduced incidence of agitation, and a decreased need for supplementary pain relief when compared to those in group C.

Additionally, our results in this study also indicated that the administration of Dex decreased the inflammatory response following cochlear implantation in younger children. It is widely recognized that local tissue edema, triggered by pharyngeal discomfort after general anesthesia, intubation, and the surgical procedure, can cause inflammatory reactions. TNF-α is an early inflammatory mediator in the inflammatory response [17], while IL-6 is a promoter of the inflammatory response [18], regulating tissue metabolic activity by altering the permeability of capillary endothelial cells [19]. Therefore, measuring serum IL-6 and TNF-α levels can indicate the extent of the inflammatory response in vivo.

Some studies have indicated that Dex inhibits the synthesis of inflammatory cytokines such as IL-6 and TNF-α by inhibiting the activation of B cell κ-light chain (NF-κB) and Toll-like receptor 4 mRNA (TLR4 messenger) through nuclear factor modulation. This reduction in the

degree of inflammatory response protects the tissues of various organs [20, 21]. Other studies have confirmed that Dex acts on the α_2-adrenoceptor in the locus coeruleus, stabilizes the capillary endothelial cell layer, reduces the permeability of capillary endothelial cells, and thus plays an anti-inflammatory role [22, 23]. In this study, we found that serum levels of IL-6 and TNF-α were elevated in both groups at the time of discharge from the PACU when compared with the preoperative phase. However, the increase in levels was more pronounced in group C, suggesting that Dex played a positive role in the anti-inflammatory process.

In this study, we also did not find any instances of respiratory depression or sinus bradycardia in group D. The reasons for this could be as follows: (1) Dex was stopped 30 min before the end of the operation, and by the time the patient was transferred out of the resuscitation room, 2–3 context sensitive halftime (t1/2CS) had already passed; (2) this outcome may be related to the inherently accelerated baseline heart rate of young children, coupled with the small sample size in the present study. This is also a limitation that needs to be addressed in future studies to substantiate the empirical findings.

This study has several limitations. Firstly, the selection of study participants was restricted by specific inclusion and exclusion criteria. For example, children with laryngeal cartilage dysplasia, sinus bradycardia or atrioventricular block were excluded. These exclusions aimed to reduce confounding factors but limited the generalizability of the results. Secondly, the sample size of 80 children, although sufficient for some analyses, may not be large enough to detect all possible effects or rare events precisely. Additionally, being a single-center study, the results may be influenced by the specific characteristics of the hospital's medical environment, staff practices, and patient population. Thirdly, the study mainly focused on a limited set of observational indexes such as MAP, HR, agitation scores (CRIES and PAED), inflammatory markers (IL −6 and TNF - α), and supplementary pain relief. Other aspects like cognitive function recovery, long-term hearing improvement, and quality of life were not comprehensively evaluated. Finally, the short-term nature of the study, observing only the anesthesia recovery period and immediate post-operative period, precluded an in-depth exploration of the long-term effects of dexmedetomidine on children's growth, development, immune system function, and long-term hearing recovery.

Conclusions

In conclusion, our results indicate that the use of Dex can reduce the occurrence and severity of agitation during recovery from anesthesia in young children following cochlear implantation surgery and improve postoperative inflammatory reactions.

Abbreviations

Dex	Dexmedetomidine
PACU	Postanesthesia care unit
MAP	Mean arterial pressure
HR	Heart rate
CRIES score	Crying, Requires increased oxygen administration, Increased vital signs, Expression and Sleeplessness score
PAED scale	Pediatric anesthesia emergence delirium scale
IL-6	Interleukin-6
TNF-α	Tumor necrosis factor-α
NYHA	New York Heart Association Functional Classification

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12871-025-02970-x.

Supplementary Material 1

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Author contributions
Conceptualization: Qing Cheng, Ze-Yu Zhao.Data curation: Qing Cheng, Chao-Yang Chen, Xiang Li, Li-Jun Wu.Formal analysis: Xiang Li, Li-Jun Wu, Ze-Yu Zhao.Funding acquisition: Qing Cheng.Roles/Writing - original draft: Qing Cheng, Chao-yang Chen.Writing - review & editing: Ze-Yu Zhao.All authors reviewed the manuscript.

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Data availability
The datasets generated and/or analysed during the current study are not publicly available but are available from the corresponding author （Ze-Yu Zhao）on reasonable request.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the declaration of Helsinki.This study was conducted with approval from the Ethics Committee of Sichuan Provincial Rehabilitation Hospital of Chengdu University of TCM (CKLL-2023004). Written informed consent was obtained from the minor(s)' legal guardian for the publication of data included in this article.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

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