ORIGINAL ARTICLE

Iran J Allergy Asthma Immunol In press.

Comparative Study of Dexmedetomidine Administration Routes in Pediatric Patients Receiving Endoscopic Low-temperature Plasma Adenotonsillar Ablation

Kaiying Song, Ling Li, Peijun Li, Xuetao Yan, Yongmei Zhao, Huiqin Lu, and Zigang Liu

Shenzhen Baoan Women's and Children's Hospital, Shenzhen, China

Received: 25 March 2025; Received in revised form: 8 August 2025; Accepted: 31 August 2025

ABSTRACT

This study aimed to explore the effects of different dexmedetomidine (DEX) administration routes on anesthesia quality in pediatric patients undergoing endoscopic low-temperature plasma adenotonsillar ablation.

We selected 120 children with obstructive sleep apnea hypopnea syndrome scheduled for surgery between May and December 2023. Participants were divided into four groups (n=30 each): a control group (Group S) receiving standard anesthesia without DEX; a local anesthesia group (Group L) receiving ropivacaine infiltration with 0.3 µg·kg⁻¹ DEX; an intravenous group (Group T) receiving 0.6 µg·kg⁻¹ DEX infusion post-induction; and a nasal drip group (Group N) receiving 0.6 µg·kg⁻¹ DEX intranasally upon room entry. We compared operation/extubation/recovery times, and scores from the Observer Assessment of Alertness and Sedation (OAA/S), Objective Pain Scale (OPS), and Pediatric Anesthesia Emergence Delirium (PAED) scales. Rescue sedation and safety were also assessed.

Group T showed lower heart rates at specific timepoints, while Group L had lower blood pressures. Recovery time (Steward score ≥4) was longer in Groups L and T compared to Group S, but not in Group N. Groups T and N showed increased OAA/S scores post-awakening, with Group N having the highest scores. OPS and PAED scores decreased in all DEX groups, with Group N demonstrating the lowest scores, followed by Group L and then Group T. No significant differences were found in operation time, extubation time, or the incidence of rescue sedation/complications among groups.

Intranasal DEX emerged as the optimal route, providing effective analgesia and sedation without prolonging recovery time.

Keywords: Adenoidectomy; Anesthesia recovery period; Child; Dexmedetomidine; Postoperative complications; Tonsillectomy

INTRODUCTION

Obstructive sleep apnea hypopnea syndrome

Corresponding Authors: Huiqin Lu, MD; Shenzhen Baoan Women's and Children's Hospital, Shenzhen, China. Tel: (+86 134) 8017 0951, Fax: (+86 134) 8017 0951, Email: kaiying156451616@hotmail.com

The first and second authors contributed equally to this study

(OSAHS) in children refers to the frequent partial or total obstruction of the upper airway during sleep, resulting in apnea or hypoventilation. This syndrome

Zigang Liu, MD;

Shenzhen Baoan Women's and Children's Hospital, Shenzhen, China. Tel: (+86 135) 1078 9878, Fax: (+86 135) 1078 9878, Empil: https://doi.org/10.1016/j.com/

1

Email: liuzigang doc@163.com

causes pathophysiological changes, such as hypoxemia and hypercapnia.^{1,2} Clinical manifestations include snoring, apnea, and mouth breathing, which are often accompanied by poor sleep quality, frequent nocturia, and sleep disturbances, as well as behavioral and attention problems in children.3 These symptoms affect not only the quality of children's sleep but also cardiovascular and multisystem functions and, in severe cases, even the growth and development of children.^{4,5} Studies have shown that the main cause of OSAHS in children is enlarged tonsils and/or adenoids. The treatment methods include general treatment (improving diet, increasing exercise, and adjusting sleep habits), drug treatment, device treatment [nasal dilator, oral appliance, or continuous positive airway pressure (CPAP)], and surgical treatment (adenoidectomy or tonsillectomy).⁶⁻⁹ The surgical removal of tonsils or adenoids is the most effective treatment. 10 Clinical symptoms are relieved in 70% of children who undergo adenoidectomy and/or tonsillectomy, significantly improves their quality of life.¹¹

In endoscopic low-temperature plasma adenotonsillar ablation, tracheal intubation and general anesthesia are commonly used. Although anesthesia techniques are relatively mature and the surgical duration is generally short, the visual and operable range of pediatric oral surgery is relatively small, and the oral mucosal blood flow is abundant, making hemostasis difficult. Poor hemostasis can lead to complications. Moreover, children have poor tolerance to ischemia, and oral mucosal bleeding can also affect the safety of intraoperative anesthesia. 12,13 Moreover, due to the immature physical and mental development of children, delays in postoperative treatment will not only affect the surgical outcome but also the health of children. Therefore, active and effective anesthesia methods for children with OSAHS are needed to ensure successful postoperative recovery.14

The insertion of endoscopes and oral surgery results in significant stimulation. Therefore, deep anesthesia is necessary to meet surgical needs and reduce fluctuations in vital signs during the operation. The use of ropivacaine for local infiltration during surgery can reduce intraoperative pain, maintain stable vital signs, alleviate stimulation, reduce the dosage of general anesthesia drugs, alleviate postoperative pain, and reduce the incidence of pain and irritability in children in the postoperative period. ¹⁵ Dexmedetomidine (DEX) is a highly effective and specific α_2 -adrenoceptor agonist

that is more selective for the α_2 -adrenoceptor than clonidine. The α_2 -adrenoceptor agonist inhibits the I_h current of the peripheral nerve, thereby hyperpolarizing the nerve. 16,17 A study has shown that DEX inhibits the inward rectifying currents of sodium and delays potassium ions in neurons, which may confer neuroprotective effects and shorten or reduce the occurrence of postoperative delirium. ¹⁸ Multiple studies have shown that DEX can improve intraoperative conditions while reducing the occurrence of emergency agitation (EA) and negative postoperative behavioral changes (NPOBCs) during the postoperative recovery period. 19,20 Recently, the use of DEX in pediatric anesthesia has improved patient comfort, the stability of vital signs during surgery, and the quality of recovery after surgery. The rational adjustment of medication is an area of international research.²¹ At present, DEX is administered by multiple routes in pediatric patients endoscopic low-temperature receiving adenoidectomy combined with tonsillectomy, and these routes include local infiltration with ropivacaine,²² intraoperative intravenous use,23 and preoperative nasal drip use.²⁴ The effects and benefits of each route of administration during and after surgery are not yet clear.

Therefore, this study presents a comparison of three different routes of DEX administration, including local infiltration anesthesia in combination with ropivacaine, intravenous DEX administration during surgery, and a nasal drip of DEX before surgery, in pediatric patients undergoing endoscopic coblation adenoidectomy combined with tonsillar ablation. The effects of the three administration routes on intraoperative blood loss, intraoperative vital signs, vital signs during the recovery period, and postoperative irritability or delirium were compared to determine the best administration route that can reduce intraoperative and postoperative bleeding, maintain stable intraoperative and postoperative vital signs, reduce the intraoperative dosage of general anesthetics, improve postoperative irritability and related complications, and improve the quality of postoperative recovery.

MATERIALS AND METHODS

Study Design

According to the inclusion criteria, 129 children were recruited, and after applying the exclusion criteria, 8 children were excluded: 3 children underwent new surgery, 1 child had severe hypertension, 3 children's

guardians requested to withdraw from the study, and 1 child's family member refused to sign an informed consent form. A total of 121 patients were randomLy assigned to the control group (Group S, 30 patients), local anesthesia group (Group L, 31 patients), intravenous group (Group T, 30 patients), or nasal drip group (Group N, 30 patients). Due to severe allergic reactions in one patient in Group L, 120 children completed the study, and their medical records were subsequently analyzed, with 30 patients in each group (Figure 1).

When the effect size is large (Cohen's f = 0.4), with the significance level (α) set at 0.05 and the statistical power (Power) set at 0.95, the required total sample size is 112 participants. In this study, the final determined sample size was 30 participants per group, with a total sample size of 120 participants. This sample size exceeds the estimated minimum required sample size, thereby providing higher statistical power for the study and further ensuring the reliability and robustness of the results.

Study Participants

This study was conducted at the research center of our hospital from May 20, 2023, to December 31, 2023, and included 120 hospitalized children with OSAHS who underwent plasma adenoidectomy combined with tonsillectomy. After a multidisciplinary consultation involving experts in otolaryngology, anesthesiology,

and pediatrics, the diagnosis of OSAHS was confirmed by ECG, chest X-ray examination, and histopathological examination.

The inclusion criteria for patients were as follows: 1) met the diagnostic criteria for OSAHS²⁵ and voluntarily underwent endoscopic low-temperature plasma adenotonsillar ablation,²⁶ with complete clinical data; 2) aged 2–12 years; 3) preoperative assessment yielded an American Society of Anesthesiologists (ASA) classification of I-II;²⁷ 4) normal coagulation function and liver function; 5) no contraindications for general anesthesia; and 6) no other ear, nose, or throat diseases. In addition, informed consent was obtained from the parents or guardians of the children.

The exclusion criteria were as follows: 1) congenital dysplasia or malformation; 2) presenting with severe liver or kidney diseases; 3) presenting with mental illness or psychological disorders; 4) presenting with hematological disorders; 5) coagulation disorders; 6) long-term use of sedatives; and 7) allergies to DEX or other anesthetic drugs.

Drop-out criteria: 1) did not meet the inclusion and exclusion criteria; 2) developed serious complications during the surgery, requiring interruption of the operation; 3) severe bleeding or coagulation problems after surgery; 4) parents or guardians requested to withdraw from the study; 5) parents or guardians of the child receiving treatment refused to sign the informed consent form; and 6) undergoing other surgeries.

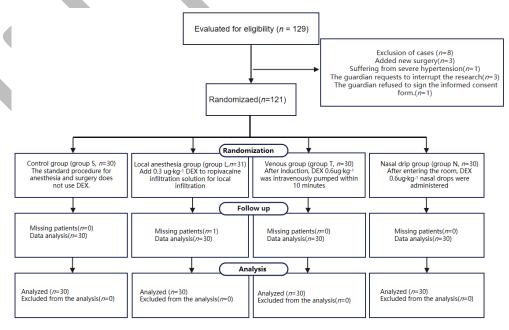


Figure 1. Design flow chart

Research Methods

Clinical information collection methods

When the children were admitted to the hospital, the integrated nursing team collected the children's general information, such as age, height, weight, and ASA classification. The recovery time (from the end of surgery to spontaneous eye opening or response to commands) and extubation time (from the completion of surgery to extubation) were recorded, and the surgical field and duration of surgery were recorded using an endoscope.

Biological Parameter Detection Methods

Heart rate (HR), blood pressure [systolic and diastolic blood pressure (SBP/DBP)], and blood oxygen saturation (SpO₂) were measured by the monitor (Manufacturer: Philips Medizin Systeme Boeblingen Gmbh. Medical Device Registration No.: CFDA(I)20143214508. Model: MX550).

Surgical Methods

The surgical procedure was endoscopic lowtemperature plasma adenoidectomy combined with tonsillar ablation. The surgical incision and procedure were completed by the same group of doctors according to a standard method. The specific operation procedure was as follows: a low-temperature plasma ablation system (Manufacturer: Chengdu Meichuang Medical Technology Co., LTD. Model: PLA-600) was used, and the ablation energy and coagulation energy output gears were set to 7 and 3 levels, respectively. The child was placed in a supine position, and after receiving general anesthesia, an opening device was used to open the child's oropharyngeal cavity. Under nasal endoscopy, a plasma knife was used to gradually separate the tonsils from the upper pole to the lower pole along the posterior membrane of the tonsils, which were completely removed. The adenoid was ablated from the top to the bottom with a plasma knife, and the ablation was stopped when the pharyngeal round pillow and pharyngeal orifice of the eustachian tube were clearly exposed. If wound bleeding occurred during the treatment, pressure was applied to stop the bleeding.

Anesthesia Method

Surgical anesthesia was induced by total intravenous endotracheal intubation general anesthesia (TIVA), and all the subjects received general anesthesia according to

a unified standard protocol as follows: for the general anesthesia plan, 100% oxygen was received for 3 minutes in advance, and 0.1 mg·kg⁻¹ dexamethasone (National Medical Products Administration H41020330, specification: 5 mg) was received intravenously before induction (maximum dose not exceeding 5 mg). Induction was performed with 2.5-4 mg/kg propofol (National Medical Products Administration H20203571, specification: 0.2 g), 3 µg/kg fentanyl (National Medical Products Administration H42022076, specification: 0.1 mg), and 0.6 mg/kg rocuronium bromide (National Medical Products Administration H20183109). After sufficient anesthesia depth was reached, endotracheal intubation was performed, and the anesthetic agent was continuously delivered by a micropump. Propofol was injected at 9-15 mg·kg⁻¹·h⁻¹, and the end tidal carbon dioxide concentration was controlled at 30-45 mmHg. Propofol (2-4 mg/kg) was injected intravenously, and 0.3 mg/kg rocuronium was added if throat reflex or swallowing occurred. The intraoperative blood pressure or HR of the patient decreased by ≥30% compared with the preoperative baseline value, and this decrease persisted for 5 minutes. An intravenous infusion of 10 mL/kg Ringer's solution (National Medical Products Administration H20043897, specification: 500 mL) or 0.01 mg/kg atropine (National Medical Products Administration H41020324, specification: 1 mL) was administered. After tonsillectomy during surgery, 0.375% ropivacaine (national drug approval number H20183109, specification: 10 mL) was used for local infiltration. Postanesthesia care was conducted at a unit with a tracheal tube after surgery.

Grouping Method

The different routes of DEX administration were divided into the following four groups: in the control group (Group S), anesthesia and surgery were performed according to standard procedures, and DEX was not used; in the local anesthesia group (Group L), 0.3 $\mu g \cdot k g^{-1}$ DEX was added to the DEX ropivacaine infiltration solution for local infiltration; in the intravenous group (Group T): 0.6 $\mu g \cdot k g^{-1}$ DEX was intravenously delivered by a pump within 10 minutes after induction; and in the nasal instillation group (Group N): the patient received 0.6 $\mu g \cdot k g^{-1}$ DEX by nasal instillation upon entering the room. To avoid observer bias, the assessors were blinded to the grouping of the participants when recording data. After data

collection was completed, an independent third party conducted data decoding and analysis.

Assessment Scales and Scoring Criteria

- (1) The Cormack–Lehane grading standard includes the following classifications:²⁸ Grade I, glottis fully exposed, anterior and posterior glottis joints are visible; Grade II, the glottis is partially exposed, and the retroglottis commissura are visible; Grade III, the glottis cannot be exposed, and the epiglottis is visible; and Grade IV, the glottis and epiglottis are not visible.
- (2) Steward recovery score:²⁹ This scale contains three items, namely, the degree of consciousness, the degree of respiratory patency, and the degree of physical activity; each item is scored on a scale of 0–2 points, and the total score is 6 points. The recovery status is proportional to the score. Note: Patients with a Steward score of 4 or higher were not allowed to leave the operating room or recovery room.
- (3) The Observer Assessment of Alertness and Anxiety Scale (OAA/S)³⁰ consists of the following criteria: Grade 1, fully awake, able to respond quickly

- and normally; Grade 2, slightly delayed response to verbal requests; Grade 3, no response to verbal requests but able to respond to loud verbal requests; Grade 4, no response to repeated loud verbal requests, requiring gentle tapping of the body to elicit a response; and Grade 5, no response from the body to normal stimuli, but there is a response to harmful stimuli. A lack of response to harmful stimuli is considered anesthetized. Typically, the required depth of sedation during surgery should reach Level 3 or 4.
- (4) Objective pain scale (OPS):³¹ Pain was assessed without the participation of the child according to blood pressure, crying, movement, irritability, and speech or body language. Each index was divided into 3 grades-0, 1, and 2 points-as shown in Table 1. A total score of≥6 indicates that analgesia is needed. See Table 1 for details.
- (5) Pediatric Anesthesia Emergence Delirium Scale (PAED):³² This scale has 5 items, and the total score is 20 points. The higher the score is, the more severe the agitation in the child.

Table 1. OPS score table

Index	0 points	1 point	2 points
Blood pressure	Increased compared to preoperative levels, but less than 10%	Increased by 10% to 20% compared to preoperative levels	Increased by 20% to 30% compared to preoperative levels
Crying	Not	Crying and responding to affection	Crying and unresponsive to love
Movement	Be quiet	Constantly moving	Tossing (jumping and jumping around)
Irritability	Sleep or quietness	Mild irritability	Hysteria
Speech or Body language	Sleep or painless treatment	Mild pain, unable to locate	Moderate pain, able to locate (referring to or say)

OPS: objective pain scale.

Indicators of Observation

The age, height, weight, preoperative HR, SBP, DBP, SpO₂, and other basic information were collected from the children. Vital signs (HR, SBP, DBP, and SpO₂) were continuously monitored before entering the operating room (T0); after 10 min (T1) and 30 min (T2) of induction maintenance during the operation; and at 10 min (T3), 20 min (T4), and 30 min (T5) after waking. The operation time, extubation time, and recovery time

(Steward score≥4) were recorded. The sedation effect (OAA/S score), postoperative pain (OPS score), and agitation during recovery (PAED score) were recorded at the time of extubation and 10 min, 20 min, and 30 min after waking. Rescue sedation and safety assessments (whether to control bleeding after surgery and whether related complications, such as laryngospasm, developed) were recorded.

Statistical Analysis

SPSS 25.0 was used to analyze the data, and the count data are presented as $[n\ (\%)]$ and were analyzed via a chi-square test. The quantitative data are presented as mean \pm SD, and t tests were used for intergroup and intragroup comparisons. One-way analysis of variance (ANOVA) was used for multigroup comparisons, with Bonferroni correction applied to control for the risk of false positives due to multiple comparisons. A p value<0.05 was considered statistically significant.

RESULTS

Clinical Data

Age, weight, height, ASA grade, SBP, DBP, HR, SpO_2 , or Cormack–Lehane grade did not significantly differ (p>0.05) among the four groups of children (Table 2).

Changes in the Vital Signs of the Patient During Surgery and after Awakening Heart Rate

The HR of the children was high before entering the

room and during the operation, but gradually decreased after resuscitation, and the HR of the N group was the lowest. The HR values in Group T were lower than those in Group S and Group N after T1 (p<0.05), those in Group T were lower than those in Groups S, L, and N at T2 (p<0.05), and those in Group N were lower than those in Group S at T4 and T5 (p<0.05). No significant difference was identified between the other two groups (p>0.05, Figure 2).

SpO₂

The SpO₂ did not significantly differ among the four groups at T0, T1, T2, T3, T4, and T5 (p>0.05, Figure 3).

Blood Pressure

Compared with that at T0, the DBP fluctuated greatly during the surgery and stabilized after the patients entered the resuscitation room. Except at timepoint T1, in Group L, this value was lower than those in the other groups (Groups S, T, and N (p<0.05). The other two groups did not significantly differ (p>0.05, Figure 4).

Table 2. Clinical Data (Mean ± SD)

Index	Group S	Group L	Group T	Group N	F	p
	(n=30)	(n=30)	(n=30)	(n=30)	value	
Age, y	5.44 ± 1.88	5.35 ± 1.33	5.19 ± 2.36	6.02 ± 1.81	1.100	0.352
Weight, kg	21.14 ± 8.05	19.05 ± 4.77	19.00 ± 7.26	21.95 ± 6.65	1.449	0.232
Height, cm	111.60 ± 16.32	112.40 ± 11.31	112.07 ± 14.81	117.70 ± 11.98	1.294	0.280
ASA, n (%)					3.025	0.388
I	29 (96.67)	30 (100.00)	30 (100.00)	30 (100.00)		
II	1 (3.33)	0 (0.00)	0 (0.00)	0 (0.00)		
Indoor SBP, mmHg	111.07 ± 8.71	108.00 ± 8.11	107.57 ± 10.48	111.83 ± 10.02	1.573	0.200
Indoor DBP, mmHg	71.07 ± 9.30	66.87 ± 8.97	67.90 ± 8.38	71.27 ± 9.07		0.125
HR upon entering the room,	116.60 ± 15.53	111.57 ± 14.54	114.67 ± 17.55	118.40 ± 21.31	0.845	0.472
beats/min						
Entrance SpO ₂ , %	99.73 ± 0.52	99.73 ± 0.52	99.53 ± 0.73	99.73 ± 0.52	0.891	0.448
Cormack-Lehane, n (%)					6.126	0.106
I	26 (86.67)	29 (96.67)	30 (100.00)	26 (86.67)		
II	4 (13.33)	1 (3.33)	0 (0.00)	4 (13.33)		

ASA: American Society of Anesthesiologists; DBP: diastolic blood pressure; HR: heart rate; SBP: systolic blood pressure; SpO₂: blood oxygen saturation.

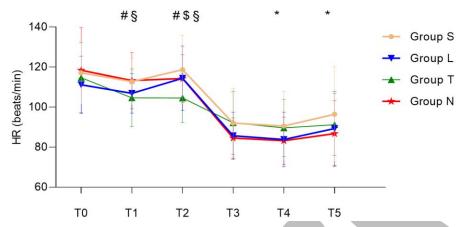


Figure 2. Changes in the heart rate (HR) of the patient during surgery and after waking up. Note: Group L compared with group S, ${}^{a}p<0.05$; Group T compared with group S, ${}^{b}p<0.05$; Group N compared with group S, ${}^{c}p<0.05$; Group T compared with group L, ${}^{c}p<0.05$; Group N compared with group T, ${}^{c}p<0.05$; Group N compared with group T, ${}^{c}p<0.05$.

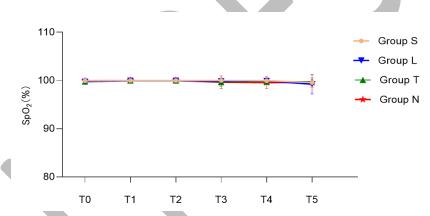


Figure 3. Changes in the peripheral oxygen saturation (SpO2) of the patient during surgery and after waking up

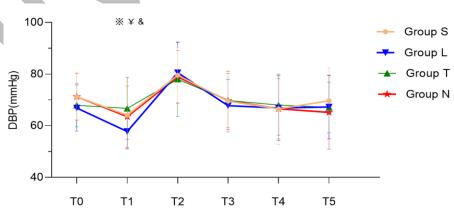


Figure 4. Changes in the diastolic blood pressure (DBP) of the patient during surgery and after waking up

Compared with that at T0, the SBP fluctuated greatly during surgery and stabilized after resuscitation. At T1, that of Group L was lower than those of Group S, Group T, and Group N, and at T2, that of Group T was lower than that of Group N (p<0.05). The other two groups did not significantly differ (p>0.05, Figure 5).

Surgical Duration, Extubation Time, and Recovery Time

Neither the surgical time nor the extubation time significantly differed among the four groups (p>0.05). Compared with Group S, the time to reach a Steward score of \geq 4 points was significantly longer in Groups L and T (p<0.05), while there was no difference in Group N; moreover, these durations were shorter in Group N than those in Groups L and T (p<0.05, Table 3).

Sedative Effect

The OAA/S scores at extubation, 10 min, 20 min, and 30 min after awakening in the four groups decreased, and the scores at 10 min, 20 min, and 30 min after awakening were lower than those at extubation (p<0.05). Compared with those in Group S, at the time of extubation and 10 min after awakening, the values in Groups T and N increased significantly, and those in Group N were greater than those in Groups T and L (p<0.05); specifically, the values were ranked as follows: Group N > Group T > Group L > Group S. At 20 min and 30 min after awakening, the values in Group N had increased (p<0.05, Table 4).

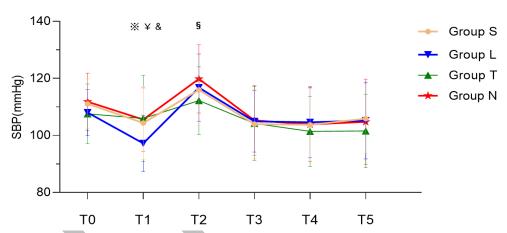


Figure 5. Changes in the systolic blood pressure (SBP) of the patient during surgery and after waking up

Group	n	Surgical duration	Extubation time	Time to Steward rating ≥4 points
Group S	30	36.83 ± 10.21	40.00 ± 14.12	56.27 ± 12.28
Group L	30	40.17 ± 10.63	44.57 ± 16.07	66.63 ± 19.44^{a}
Group T	30	37.50 ± 10.89	42.70 ± 12.52	65.10 ± 17.48^{a}
Group N	30	38.50 ± 9.21	40.30 ± 15.72	$56.37 \pm 17.88^{b,c}$
F value		0.600	0.646	3.202
p value		0.616	0.587	0.026

Table 3. Time of surgery, extubation, and Steward score ≥4 (Mean ± SD, min)

 $^{{}^{\}rm a}{\rm Compared\ with\ group\ S}, p{<}0.05, {}^{\rm b}{\rm Compared\ with\ group\ L}, p{<}0.05, {}^{\rm c}{\rm Compared\ with\ group\ T}, p{<}0.05.$

Table 4. Postoperative OAA/S score comparison (Mean ± SD, score)

Group	n	At the time of extubation	10 minutes after waking up	20 minutes after waking up	30 minutes after waking up
Group S	30	2.57 ± 0.73	1.73 ± 0.94^{d}	1.40 ± 0.62^d	1.03 ± 0.18^{d}
Group L	30	2.90 ± 0.99	2.13 ± 1.22^{d}	1.63 ± 1.00^{d}	$1.37\pm0.89^{a,d}$
Group T	30	$3.07\pm1.10^{\mathrm{a}}$	$2.27\pm1.11^{\mathrm{a,d}}$	$1.83 \pm 0.99^{a,d}$	$1.33\pm0.66^{\rm d}$
Group N	30	$3.67\pm0.96^{a,b,c}$	$2.83\pm0.83^{a,b,c,d}$	$2.03\pm0.41^{\mathrm{a},d}$	$1.47\pm0.51^{a,d}$
F value		7.341	5.744	3.495	2.749
p value		< 0.001	0.001	0.018	0.046

^aCompared with group S, p<0.05, ^bCompared with group L, p<0.05, ^cCompared with group T, p<0.05, ^dCompared with the extubation in this group, p<0.05, OAA/S: Observer Assessment of Alertness and Anxiety Scale.

Postoperative Pain

The OPS scores of the four groups decreased from extubation to 10 min, 20 min, and 30 min after awakening, and the scores at 10 min, 20 min, and 30 min after awakening were lower than those at extubation (p<0.05). Compared with those in Group S, at the time of extubation and 10 min after awakening, the scores in groups L and N were lower (p<0.05). At 20 min and 30 min after awakening, the scores in Groups L, N, and T were significantly lower than those in Group S (p<0.05); specifically, the values were ranked as follows: Group N<Group L<Group T<Group S (Table 5).

Restlessness

The PAED scores at extubation, 10 min, 20 min, and 30 min after awakening in the four groups decreased in turn, and the scores at 10 min, 20 min, and 30 min after awakening were lower than those at extubation (p<0.05). Compared with those in Group S, at the time of extubation and 30 min after awakening, the scores in groups L, N, and T were lower (p<0.05). At 10 min and

20 min after awakening, the values of Groups L and N were significantly lower than those in Group S (p<0.05); specifically, the values were ranked as follows: Group N<Group L<Group T<Group S (Table 6).

Remedial Sedation Conditions

In this study, rescue sedation was administered to 2 patients in the control group (Group S), 3 patients in the local anesthesia group (Group L), 2 patients in the intravenous group (Group T), and 0 patients in the nasal drop group (Group N), corresponding to incidences of 6.67%, 10.00%, and 0.00%, respectively. The frequency of rescue sedation did not significantly differ among the four groups (χ^2 =2.882, p=0.410).

Safety Assessment

None of the patients in any group developed postoperative bleeding, and there was no need to control bleeding; moreover, related complications, such as laryngeal spasm, nausea, or vomiting, did not occur.

Table 5. Postoperative OPS Scores (Mean ± SD, score)

Group	n	At the time of extubation	10 minutes after waking up	20 minutes after waking up	30 minutes after waking up
Group S	30	3.67 ± 2.44	2.37 ± 1.92^{c}	2.20 ± 1.86^c	2.07 ± 2.20^{c}
Group L	30	$2.43\pm2.05^{\mathrm{a}}$	$1.20\pm1.49^{\mathrm{a,c}}$	$0.50\pm1.17^{\text{a,c}}$	$0.33\pm0.80^{\mathrm{a,c}}$
Group T	30	3.13 ± 2.70	1.60 ± 1.73^{c}	$0.90\pm1.24^{\text{a,c}}$	$0.67\pm0.99^{a,c}$
Group N	30	$1.60\pm1.35^{a,b}$	$0.87\pm1.04^{\text{a,c}}$	$0.37 \pm 0.61^{\text{a,c}}$	$0.27\pm0.58^{a,c}$
F value		4.989	5.000	12.436	12.479
p value		0.003	0.003	< 0.001	<0.001

^aCompared with group S, p<0.05, ^bCompared with group T, p<0.05, ^cCompared with the extubation in this group, p<0.05. OPS: objective pain scale.

Table 6. Postoperative PAED scores (Mean ± SD, score)

Group	n	At the time of	10 minutes after	20 minutes after	30 minutes after
		extubation	waking up	waking up	waking up
Group S	30	13.30 ± 3.40	$9.20\pm4.56^{\rm c}$	6.60 ± 4.74^c	4.37 ± 3.87^c
Group L	30	$10.00 \pm 3.73^{\rm a,c}$	$6.07 \pm 4.50^{\mathrm{a,c}}$	$3.50\pm3.98^{a,c}$	$1.57\pm2.96^{\mathrm{a,c}}$
Group T	30	$11.37 \pm 4.02^{\mathrm{a,c}}$	7.40 ± 4.48^c	4.83 ± 4.61^c	$2.27\pm3.25^{\mathrm{a,c}}$
Group N	30	$8.37\pm3.95^{\mathrm{a,c}}$	$5.10\pm3.79^{\mathrm{a,c,c}}$	$2.37\pm2.77^{\mathrm{a,c,c}}$	$0.83\pm1.53^{\mathrm{a,c}}$
F value		9.171	4.803	5.919	7.593
p value		< 0.001	0.003	0.001	< 0.001

^aCompared with group S, p<0.05, ^cCompared with group T, p<0.05, ^dCompared with the extubation in this group, p<0.05, PAED: Pediatric Anesthesia Emergence Delirium Scale.

DISCUSSION

Endoscopic low-temperature plasma adenotonsillar ablation is an effective method for treating pediatric OSAHS. However, anesthesia management during surgery is crucial for the postoperative recovery of patients. Anesthesia management not only needs to ensure the safety of the surgery but also needs to minimize the occurrence of postoperative stress reactions and complications.³³ At present, the sedatives commonly used for pediatric patients before surgery include midazolam and ketamine.34,35 However, these drugs often have the risk of causing respiratory depression, delirium, increased secretions, and delayed postoperative awakening, leading to generally low acceptance in children, which seriously affects the clinical efficacy and widespread application of these drugs. Therefore, we need to find a preoperative sedative drug that is easy to use, has few side effects, and is easily accepted by children. DEX can produce sedative, analgesic, and anti-sympathetic effects. The sedation from DEX is also easily reversible, has no significant inhibitory effect on respiration, and has neuroprotective effects. It can reduce apoptosis and has high safety in clinical applications.³⁶ However, the effect of the route of DEX administration on the quality of anesthesia remains unclear. Therefore, this study presents an exploration of the effects of different administration routes of DEX on anesthesia quality in pediatric patients receiving endoscopic low-temperature plasma adenoidectomy combined with tonsillectomy to provide new ideas for clinical anesthesia.

HR and blood pressure are important physiological indicators for evaluating the health status of children and have a significant impact on their health.³⁷ This study revealed that the HR of children was high before they

entered the operating room and during the surgery; however, it gradually decreased and remained stable after awakening, and the HR of Group N was the lowest. After 10 minutes of anesthesia maintenance, the level in Group T was lower than that in Groups S and N. minutes of anesthesia Furthermore, after 30 maintenance, the level in Group T was lower than that in Groups S, L, and N, which may be due to the rapid distribution of intravenous drugs (Group T) throughout the body via the bloodstream, which acts on the central system.³⁸ However, nasal and nervous administration (Group L) resulted in slow drug absorption, a low blood drug concentration, an increased drug distribution volume, and mild cardiovascular inhibition. However, nasal drip administration (Group N) after awakening may have a reduced effect on HR because of the gradual entry of DEX into the bloodstream after absorption through the nasal mucosa, which has a certain regulatory effect on the cardiovascular system.³⁹ In addition, the duration of action of DEX after intranasal administration is relatively long, gradually stabilizing the HR of the patient. 40 This study also revealed that the DBP and SBP briefly increased during surgery compared with before the patient entered the room, and the decrease tended to stabilize after awakening. Blood pressure increases briefly at the beginning and then continues to decrease for long periods, mainly because DEX has a biphasic effect on blood pressure, from peripheral α₂-receptor activation to central α_2 -receptor activation. 41,42 In addition, the blood pressure of Group L was significantly lower than that of Group S, Group T, and Group N, except during the maintenance of anesthesia, which may be due to the local infiltration of DEX (Group L) during the maintenance of anesthesia. Specifically, DEX inhibits local nerve endings, reduces the degree of

pain stimulation in the surgical area, and thus reduces the stress response of the cardiovascular system.⁴³ However, the venous group (Group T) presented a blood pressure after 20 minutes of anesthesia maintenance, which may be related to the systemic effect of DEX after intravenous administration. In addition, the trauma of the surgery, such as bleeding and blood transfusions, as well as the surgery itself, impacts vital signs. In particular, children have immature physiological systems; therefore, their stress response to surgical trauma is stronger, resulting in large fluctuations in vital signs. However, most of the changes in vital signs were within the acceptable range, and no serious abnormalities in vital signs were observed.44 HR and blood pressure differ in individuals and among children of different age groups.⁴⁵ Therefore, further evaluation is needed to determine whether decreases in HR and blood pressure have adverse effects on affected children.

Sedation usually refers to the use of drugs or other means to reduce or eliminate the patient's pain, anxiety, or discomfort so that the patient is in a quiet, relaxed state, which allows the necessary diagnostic or therapeutic procedures to be performed, results in the appropriate degree of amnesia or decreased consciousness, and ensures the patient's safety.⁴⁵ This study revealed that, compared with Group S, Group N increased significantly at the time of extubation and at each time point after awakening. These results indicate that different routes of DEX administration effectively produce sedation, with intranasal administration being the most effective route of administration. hypothesize that this finding is related to the pharmacological action of DEX, which activates α2adrenergic presynaptic receptors in the locus coeruleus of the brain, inhibits norepinephrine release, terminates pain signaling, and induces a sedative effect very similar to that of natural NREM sleep. 46 The half-life of DEX clearance is approximately 2-3 hours. Tonsillectomy surgery is rapid, and DEX can still provide appropriate sedative and analgesic effects during the recovery period.⁴⁷ Nasal drip administration benefits from its high drug absorption efficiency and reduces postoperative pain and other stress reactions, which helps maintain a stable sedative state and improves sedative effects. This study revealed that nasal drip administration does not prolong the recovery time of children, whereas intravenous and local anesthesia administration may prolong the recovery time to some extent.

Emergence agitation often occurs in the early stage of anesthesia recovery, and its clinical manifestations are related to age, surgical method, anesthesia time, and other risk factors. 48 Studies have shown that agitation during the awakening period has a shorter onset, but if not controlled in a timely manner, it can cause serious complications in the circulatory and respiratory systems, which is associated with a poor prognosis. Postoperative pain is a common complication in children after surgery and has a negative impact on their recovery and quality of life. Therefore, agitation during anesthesia recovery and postoperative pain urgently need to be reduced to improve the prognosis in surgical patients. In this study, the effects of different routes of DEX administration on restlessness and pain in children during the recovery period were investigated. Compared with those of Group S, the PAED and OPS scores of the other three groups decreased after recovery; those of Group N were the lowest, specifically, lower than those of Group S. Different routes of DEX administration alleviated agitation during the recovery period and postoperative pain in children, and nasal drip administration had the most significant antiagitation and analgesic effects, primarily because DEX is an α₂-adrenergic receptor agonist that acts on the peripheral and central nervous systems of the body, stimulating α_2 -adrenergic receptors on the postsynaptic membrane. 49 It also inhibits neuronal firing and neurotransmitter release, thereby exerting sedative, analgesic, and anti-anxiety effects and reducing agitation during anesthesia recovery. In addition, DEX blocks the release of norepinephrine and reduces sympathetic nervous tension, effectively blocking pain transmission and reducing pain. 50 Nasal drip administration is a noninvasive, painless, and convenient method to deliver medication that avoids the pain and risk of infection that may be caused by intravenous injection and reduces the pain and stress response of children.⁵¹ In addition, nasal drip agents directly enter the bloodstream through the nasal mucosa and exert therapeutic effects, avoiding delays in systemic circulation and reducing the occurrence of agitation during the recovery period in children.

This study revealed no significant differences in surgical duration or extubation time among the groups. These findings indicate that different routes of DEX administration have little effect on surgical time or extubation time and do not increase surgical risk or extubation difficulty. In addition, salvage sedation or adverse reactions did not significantly differ between the

different DEX administration routes, perhaps because the predictability of surgical duration allowed surgeons to operate while the patient was optimally sedated. Moreover, predictable extubation times allow children to quickly recover spontaneous breathing after surgery, reducing the occurrence of complications.⁵²

The findings of this study are subject to several limitations. The sample size was relatively small, and the study was conducted at a single center. The experimental results may have certain biases and random errors. It is noteworthy that the small sample size may limit our ability to detect rare adverse reactions. Therefore, largerscale studies are needed in the future to further validate the safety of this experiment. In addition, we did not further stratify the included children by age to evaluate the impact of DEX on postoperative recovery across different age groups, which may obscure age-specific effects of DEX. Although we made every effort to ensure that there were no statistically significant differences in basic characteristics among the groups, we did not further adjust for these potential confounding factors through multivariate regression analysis. This could potentially affect the interpretation of the results, particularly when evaluating the impact of different drug administration routes on the quality of anesthesia.

While our study aimed to compare the efficacy of different routes of DEX administration, a critical limitation must be acknowledged. The dosage of DEX was not consistent across all intervention groups; the Group L received 0.3 µg·kg⁻¹, while the intravenous and nasal instillation groups received 0.6 µg·kg⁻¹. This discrepancy introduces a significant confounding variable. Consequently, any observed differences in outcomes, such as superior analgesia or sedation in Group N, cannot be definitively attributed to the nasal route itself. It is plausible that the effects seen in Groups T and N are simply a function of the higher systemic dose. Therefore, the conclusion that nasal instillation is a superior route of administration is not fully supported by the present study design. Future research employing equivalent DEX doses across all administration routes is essential to isolate and accurately compare the true effect of the route of administration.

Second, this study only involved the investigation of the impact of different administration routes of DEX on anesthesia quality and did not involve an evaluation of the long-term prognosis in patients. To increase the reliability and accuracy of the experiment, we will consider expanding the sample size, optimizing the experimental design, or adopting more advanced statistical methods to reduce the influence of bias and random error to comprehensively evaluate the impact of different routes of DEX administration on the anesthesia quality and long-term prognosis in children. Moreover, we will explore the combined application of DEX with other anesthetic drugs and further explore the mechanisms and effects of different routes of DEX administration, providing more accurate and effective guidance for clinical anesthesia.

In summary, DEX can reduce the severity of pain and agitation during the recovery period after pediatric endoscopic low-temperature plasma adenotonsillar ablation in children and increase sedative effects. The best route of administration is a nasal drip, which does not increase the recovery time in children and is highly safe. Therefore, the use of DEX nasal drops in pediatric patients receiving low-temperature plasma adenoidectomy combined with tonsillectomy should be prioritized. However, attention should be given to monitoring changes in the child's vital signs to ensure patient safety.

STATEMENT OF ETHICS

This experiment was approved by Shenzhen Baoan Women's and Children's Hospital Ethics Committee (Ethics Approval Number: LLSCHY-2023-01-04-02).

FUNDING

Supported by the High-level Medical Team Project in Baoan, Shenzhen (No. 202404).

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGMENTS

Not applicable.

DATA AVAILABILITY

Data supporting this study's findings are available from the corresponding author (Huiqin Lu; kaiying156451616@hotmail.com) upon reasonable request.

AI ASSISTANCE DISCLOSURE

This manuscript was prepared without the assistance of AI.

REFERENCES

- Lv R, Zhao Y, Wang Z, Liu X, Wang Z, Li S, et al.
 Obstructive sleep apnea hypopnea syndrome in ancient traditional Chinese medicine. Sleep Breath. 2023;27(4):1597-610.
- Iannella G, Magliulo G, Greco A, de Vincentiis M, Ralli M, Maniaci A, et al. Obstructive Sleep Apnea Syndrome: From Symptoms to Treatment. Int J Environ Res Public Health. 2022;19(4).
- 3. Zeng GH, Xu G, Liu HY, Gao Z. Association between mean platelet volume and obstructive sleep apnea-hypopnea syndrome in children. Medicine (Baltimore). 2022;101(43):e31505.
- 4. Shi N, Pang F, Chen J, Lin M, Liang J. Abnormal interaction between cortical regions of obstructive sleep apnea hypopnea syndrome children. Cereb Cortex. 2023;33(19):10332-40.
- 5. Hosseini HR, Ngan P, Tai SK, Andrews LJ 2nd, Xiang J. A comparison of skeletal and dental changes in patients with a Class II relationship treated with clear aligner mandibular advancement and Herbst appliance, followed by comprehensive orthodontic treatment. Am J Orthod Dentofacial Orthop. 2024;165(2):205-19.
- Rueda JR, Mugueta-Aguinaga I, Vilaró J, Rueda-Etxebarria
 M. Myofunctional therapy (oropharyngeal exercises) for
 obstructive sleep apnoea. Cochrane Database Syst Rev.
 2020;11(11):CD013449.
- Combs D, Edgin J, Hsu CH, Bottrill K, Van Vorce H, Gerken B, et al. The combination of atomoxetine and oxybutynin for the treatment of obstructive sleep apnea in children with Down syndrome. J Clin Sleep Med. 2023;19(12):2065-73.
- Abijay CA, Tomkies A, Rayasam S, Johnson RF, Mitchell RB. Children with Down syndrome and obstructive sleep apnea: outcomes after tonsillectomy. Otolaryngol Head Neck Surg. 2022;166(3):557-64.
- 9. Ashrafizadeh M. Cell death mechanisms in human cancers: molecular pathways, therapy resistance and therapeutic perspective. J Cancer Biomol Ther. 2024;1(1):17-40.
- 10. Liu Z, Li S, Mu S, Yang Z, Li J, Ding L, et al. The efficacy of cryogenic plasma tonsillectomy in the treatment of obstructive sleep apnea-hypopnea syndrome in children: a meta-analysis. Pediatr Pulmonol. 2023;58(3):834-43.

- 11. Zhong J, Luo X, Qiu S, Cheng C, Zhou Y, Chen L, et al. Preliminary study on efficacy and safety of submucosal plasma ablation of inferior turbinate in children with allergic rhinitis complicated with obstructive sleep apnea syndrome. J Clin Otorhinolaryngol Head Neck Surg. 2022;36(10):758-62.
- Varadharajan K, Caton N, Faulkner J, Khemani S. Coblation intracapsular tonsillectomy in children with recurrent tonsillitis: initial experience. Int J Pediatr Otorhinolaryngol. 2020;135:110113.
- 13. Wu Y, Zhang N, Wang L, Zhang Q, Yuan Q, Wang X, et al. Effect of tonsillotomy on the inflammation and immune function in children with chronic tonsillitis. J Clin Otorhinolaryngol Head Neck Surg. 2023;37(4):297-301.
- 14. St Rose T, Carr SN, Phillips AK, Reeder NP, Relf MV. Improving identification of pediatric emergence delirium in the post anesthesia care unit: a quality improvement opportunity. J Perianesth Nurs. 2022;37(6):770-3.
- 15. Bhardwaj S, Devgan S, Sood D, Katyal S. Comparison of local wound infiltration with ropivacaine alone or ropivacaine plus dexmedetomidine for postoperative pain relief after lower segment cesarean section. Anesth Essays Res. 2017;11(4):940-5.
- 16. Duan S, Zhou S. Dexmedetomidine and perioperative arrhythmias. J Cardiothorac Vasc Anesth. 2024;38(5):1221-7.
- 17. Persson N, Uusalo P, Nedergaard M, Lohela TJ, Lilius TO. Could dexmedetomidine be repurposed as a glymphatic enhancer? Trends Pharmacol Sci. 2022;43(12):1030-40.
- 18. Lin J, Wu C, Zhao D, Du X, Zhang W, Fang J. The sedative effects of inhaled nebulized dexmedetomidine on children: a systematic review and meta-analysis. Front Pediatr. 2022;10:865107.
- 19. Zhao GG, Lou C, Gao RL, Lei FX, Zhao J. Combined use of dexmedetomidine and nalbuphine in laparoscopic radical gastrectomy for gastric cancer. World J Gastrointest Oncol. 2024;16(7):2952-9.
- 20. Lee-Archer P, McBride C, Paterson R, Reade M, Reglivon Ungern-Sternberg B, Long D. Does dexmedetomidine given as a premedication or intraoperatively reduce post-hospitalisation behaviour change in children? A study protocol for a randomised controlled trial in a tertiary paediatric hospital. BMJ Open. 2018;8(4):e019915.
- 21. Shioji N, Everett T, Suzuki Y, Aoyama K. Pediatric sedation using dexmedetomidine and remimazolam for magnetic resonance imaging. J Anesth. 2022;36(1):1-4.
- 22. Hao J, Wu Z, Luo Z, Dong B. Addition of dexmedetomidine to ropivacaine for local infiltration anaesthesia improves analgesic efficacy after

- tonsillectomy and adenoidectomy: a randomized controlled trial. Int J Pediatr Otorhinolaryngol. 2020;137:110168.
- 23. Zhang T, Li H, Lin C, An R, Lin W, Tan H, et al. Effects of an intraoperative intravenous bolus dose of dexmedetomidine on postoperative catheter-related bladder discomfort in male patients undergoing transurethral resection of bladder tumors: a randomized, double-blind, controlled trial. Eur J Clin Pharmacol. 2024;80(3):465-74.
- 24. He J, Zhang X, Li C, Fu B, Huang Y, Li H. Dexmedetomidine nasal administration improves perioperative sleep quality and neurocognitive deficits in elderly patients undergoing general anesthesia. BMC Anesthesiol. 2024;24(1):42.
- 25. Pateron B, Marianowski R, Monteyrol PJ, Couloigner V, Akkari M, Chalumeau F, et al. French Society of ENT (SFORL) guidelines (short version) on the roles of the various treatment options in childhood obstructive sleep apnea-hypopnea syndrome. Eur Ann Otorhinolaryngol Head Neck Dis. 2018;135(4):265-8.
- Randall DA. Current indications for tonsillectomy and adenoidectomy. J Am Board Fam Med. 2020;33(6):1025-30.
- Lew MW, Pozhitkov A, Rossi L, Raytis J, Kidambi T. Machine learning algorithm to perform the American Society of Anesthesiologists physical status classification. Cureus. 2023;15(10):e47155.
- 28. El-Tawansy A, Mohamed Salama Elnajar A, Abdel Baky Mahmoud H, Ibrahim Amin M, Abd Elmohsen Bedewy A. Validity of airway ultrasound in correlation with Cormack-Lehane grading in obese patients: a cross-sectional study. Anesth Pain Med. 2024;14(2):e142701.
- Zhou Y, Xu Z, Liu X, Liu Z, An L, Zhang S, et al. Application of TCM nursing in post-anesthesia recovery room under integrated management mode. Altern Ther Health Med. 2024;AT8395-AT.
- Nakamura H, Makiguchi T, Yamada Y, Sakurai K, Tsunoda A, Tomaru N, et al. Surgery with peripheral nerve block under dexmedetomidine sedation for foot ulcer. Plast Reconstr Surg Glob Open. 2024;12(11):e6333.
- Abduallah MA, Al-Ahwal LA, Ahmed SA. Effect of erector spinae plane block on postoperative analysis after pediatric hip surgery: randomized controlled study. Pain Pract. 2022;22(4):440-6.
- Lütze C, Weber TP, Lücke T, Gude P, Georgevici AI. Incidence of emergence delirium after homeostasis-guided pediatric anesthesia for ear-nose-throat surgery. Minerva Anestesiol. 2024;90(7-8):644-53.

- Tomas VG, Hollis N, Ouanes JP. Regional anesthesia for vascular surgery and pain management. Anesthesiol Clin. 2022;40(4):751-73.
- 34. Guilliams KP, Harrar D. Ketamine for status epilepticus in children: searching for the right drug for the right patient. Neurocrit Care. 2024;40(1):45-7.
- Vasakova J, Duskova J, Lunackova J, Drapalova K, Zuzankova L, Starka L, et al. Midazolam and its effect on vital signs and behavior in children under conscious sedation in dentistry. Physiol Res. 2020;69(Suppl 2):S305-14
- 36. Lim JY, Ker CJ, Lai NM, Romantsik O, Fiander M, Tan K. Dexmedetomidine for analgesia and sedation in newborn infants receiving mechanical ventilation. Cochrane Database Syst Rev. 2024;5(5):CD012361.
- 37. Tan I, Barin E, Butlin M, Avolio AP. Relationship between heart rate and central aortic blood pressure: implications for assessment and treatment of isolated systolic hypertension in the young. Minerva Med. 2022;113(5):807-16.
- Tisotti T, Valverde A, Hopkins A, O'Sullivan ML, Hanna B, Arroyo L. Use of intravenous lidocaine to treat dexmedetomidine-induced bradycardia in sedated and anesthetized dogs. Vet Anaesth Analg. 2021;48(2):174-86.
- Lu Y, Peng C, Xie L, Wu Y, Gu L, Li S. Nasal drip of dexmedetomidine for optimal sedation during PICC insertion in pediatric burn care. Medicine (Baltimore). 2023;102(6):e32831.
- 40. Wilkens HL, Neudeck S, Kästner SB. Nasal and tracheobronchial nitric oxide production and its influence on oxygenation in horses undergoing total intravenous anaesthesia. BMC Vet Res. 2022;18(1):134.
- 41. Ke J, Pen X. The effect of dexmedetomidine on postoperative blood pressure after controlled hypotension in endoscopic sinus surgery. J Clin Otorhinolaryngol Head Neck Surg. 2013;27(10):478-80.
- 42. Dong R, Li F, Li B, Chen Q, Huang X, Zhang J, et al. Effects of an early intensive blood pressure-lowering strategy using remifentanil and dexmedetomidine in patients with spontaneous intracerebral hemorrhage: a multicenter, prospective, superiority, randomized controlled trial. Anesthesiology. 2024;141(1):100-15.
- 43. Bala R, Arora V, Anshul A, Arora R, Kamal K, Malhan S. A comparative study of intravenous dexmedetomidine with local infiltration of ropivacaine in attenuation of stress response to skull pin insertion in craniotomies. Asian J Neurosurg. 2022;17(3):463-9.
- 44. Kovoor JG, Bacchi S, Stretton B, Gupta AK, Lam L, Jiang M, et al. Vital signs and medical emergency response

- (MER) activation predict in-hospital mortality in general surgery patients: a study of 15 969 admissions. ANZ J Surg. 2023;93(10):2426-32.
- 45. Ramgopal S, Sepanski RJ, Crowe RP, Martin-Gill C. External validation of empirically derived vital signs in children and comparison to other vital signs classification criteria. Prehosp Emerg Care. 2024;28(2):253-61.
- 46. Carnet Le Provost K, Kepp O, Kroemer G, Bezu L. Trial watch: dexmedetomidine in cancer therapy. Oncoimmunology. 2024;13(1):2327143.
- 47. Chang ET, Certal V, Song SA, Zaghi S, Carrasco-Llatas M, Torre C, et al. Dexmedetomidine versus propofol during drug-induced sleep endoscopy and sedation: a systematic review. Sleep Breath. 2017;21(3):727-35.
- 48. Shenvi C, Kennedy M, Austin CA, Wilson MP, Gerardi M, Schneider S. Managing delirium and agitation in the older emergency department patient: the ADEPT tool. Ann Emerg Med. 2020;75(2):136-45.
- 49. Advances in combination therapy for gastric cancer: integrating targeted agents and immunotherapy. Adv Clin Pharmacol Ther. 2024;1(1):1-15.
- Zhuang K, Yang HT, Long YQ, Liu H, Ji FH, Peng K. Dexmedetomidine and acute kidney injury after noncardiac surgery: a meta-analysis with trial sequential analysis. Anaesth Crit Care Pain Med. 2024;43(3):101359.
- 51. Long X, Wen LX, Yang H, Zhu GH, Zhang QY, Jiang JJ, et al. ED95 of remimazolam in nasal administration for attenuating preoperative anxiety in children. Front Med. 2023;10:1253738.
- 52. Jin Y, Shen L, Ye R, Zhou M, Guo X. Development and validation of a novel score for predicting perioperative major adverse cardiovascular events in patients with stable coronary artery disease undergoing noncardiac surgery. Int J Cardiol. 2024;405:131982.

