EGYPTIAN JOURNAL OF ANAESTHESIA
2022, VOL. 38, NO. 1, 317–323
https://doi.org/10.1080/11101849.2022.2079901

The effect of nebulized dexmedetomidine as sedative premedication in pediatrics undergoing cochlear implantation

Rania M Ali and Noura M. Youssri Mahmoud

Department of Anesthesia, Intensive Care and Pain Management, Faculty of Medicine, Ain Shams University, Cairo, Egypt

ABSTRACT

Background: Sedation is crucial part of the management of cochlear implant surgery. Preoperative anxiety is more aggravated in deaf children due to limited communication. The aim of the present study was to investigate the efficacy and safety of two different doses of nebulized dexmedetomidine in deaf children undergoing cochlear implantation.

Patients and Methods: Fifty patients undergoing cochlear implantation were randomly allocated into two equal groups, D3 and D4, and were premedicated by nebulized three and four µg/kg dexmedetomidine, respectively, 30 min before induction of anesthesia.

Results: The depth of sedation in D4 group was comparable with that of D3 group. The onset of sedation and the time to maximum sedative effect were significantly earlier in D4 than in D3 group. BIS score at admission to operating theater was significantly lower in D4 than in D3 group. The level of parental separation anxiety, the degree of ease of venipuncture, and the severity level of emergence agitation were comparable in both groups. The quality of surgical field was significantly better, and the recovery time was significantly shorter in D4 group than in D3 group. The level of heart rate and mean blood pressure were significantly lower, and the rate of bradycardia and hypotension were significantly higher in D4 group than in D3 group.

Conclusions: Premedication by each of three and four µg/kg of nebulized dexmedetomidine provides a satisfactory sedation level that facilitate parental separation and intravenous cannulation, but three µg/kg was superior because it was associated with lower frequency of side effects.

ARTICLE HISTORY
Received 5 April 2022
Revised 6 May 2022
Accepted 10 May 2022

KEYWORDS
Cochlear implantation; dexmedetomidine; nebulization; pediatrics; sedation

1. Introduction

Sedation is crucial part of the management of cochlear implant surgery. Over half of the pediatric patients develop preoperative anxiety [1] which is more aggravated in deaf children due to limited communication and reassurance facilities [2].

Dexmedetomidine is a centrally acting selective α-2 adrenergic agonist with both sedative and analgesic effects with minimal respiratory depressant effect [3]. Dexmedetomidine can be used in pediatric patients for procedural sedation and premedication [4]. The sedative effect of dexmedetomidine is concentration dependent [5]. Previous studies have investigated intravenous dexmedetomidine in a dose of 1–4 µg/kg without any significant side effects [6,7]. Moreover, non-intravenous administration is usually unrelated to hemodynamic compromise [8].

Inhalation of nebulized drug is noninvasive and associated with high bioavailability [9]. Till now, there is no investigation on the administration of nebulized dexmedetomidine as sedative premedication in deaf children. So, the aim of the present study was to investigate two different doses of nebulized dexmedetomidine regarding the quality of sedation and potential side effects to find out the least effective dose in deaf children undergoing cochlear implantation.

2. Patients and methods

The Medical Ethical Committee in Ain Shams University approved this double blind prospective randomized clinical trial. Trial registration number is FMASU R 100/2021. The trial was conducted in Ain Shams University hospitals on 50 patients aged 1–8 years with American Society of Anesthesiologist physical status (ASA- ps) class I and II undergoing cochlear implantation under general anesthesia from May 2021 to February 2022. Abnormal BMI percentile for age was classified as ASA II [10].

A written informed consent was obtained from every patient's parent or legal guardian after explaining the procedure. Exclusion criteria included suspected difficult airway or body mass index > 30 Kg/m^2, children with congenital syndromes or mental retardation or neurobehavioral disorders or history of allergic reactions to Dexmedetomidine.

CONTACT Rania M Ali rania_m_ismail@yahoo.com Department of Anesthesia, Intensive Care and Pain Management, Faculty of Medicine, Ain Shams University, 38 Abbassia, Cairo, 1181 Egypt

All patients were fasting 6 h preoperatively except for clear fluids 2 h only. In the preoperative holding area, heart rate (HR), mean blood pressure (MBP) and peripheral blood oxygen saturation (SpO_2) were measured immediately before dexmedetomidine nebulization (Baseline values) then at 10, 20 and 30 min after the end dexmedetomidine nebulization.

According to the sedative dose of dexmedetomidine, patients were allocated in a randomized manner by sealed envelope method into two equal groups (D3 and D4 groups; each 25 patients). D3 group received 3 μg/kg dexmedetomidine and D4 group received 4 μg/kg dexmedetomidine. Both doses were diluted with 0.9% normal saline to total volume of three milliliter and administered via jet nebulizers through a mouthpiece (for above 3 years children) or mask (for 3 years or below children) using a continuous flow of 100% O2 at 6 L/min until dexmedetomidine in the nebulizer cup is gone. The child was in the mother's lap during dexmedetomidine administration. All study drugs were prepared and administered by an independent investigator not involved in the observation or administration of anesthesia for the children.

Sedation level was assessed at the same time schedule using the Sedation Scale (SS-5) [11]. 1 = Rarely awake, needs shaking to wake up, 2 = Asleep, eyes closed, wake up when lightly touched, 3 = Sleepy, but eyes open spontaneously, 4 = Awake, and 5 = Agitated. The onset of sedation, the minimum time interval necessary to achieve a SS-5 score of 3, and time to Peak sedative effect, the time interval from drug administration to reaching maximum level of sedation, were recorded.

Parental separation was evaluated 30 min after the end of dexmedetomidine administration using parental separation anxiety scale (PSAS). PSAS is a 4-point scale as follows: 1 = easy separation, 2 = whimpers, but is easily reassured, 3 = cries and cannot be easily reassured, but not clinging to parents, and 4 = crying and clinging to parents. Dashiff C and Weaver [12] recommend the following scoring criteria, which were used in this study: a PSAS score of 1 or 2 was classified as an acceptable separation, whereas scores of 3 or 4 were considered difficult separations from the parents.

On child admission to operating theater, patient's sedation level was recorded using Bispectral index (BIS). Also, patient's hemodynamics (HR, MAP and SPO_2) were measured before induction of anesthesia and continuously throughout the procedure. The hemodynamic data immediately after induction of anesthesia, the minimum and maximum readings throughout the operation were recorded.

An intravenous access was secured. Ease of venipuncture (EVP) was graded as poor (uncooperative without success), fair (uncooperative with success), good (minor resistance) or excellent (no reaction) [8].

0.15 mg/kg dexamethasone was given for prevention of postoperative nausea and vomiting. Induction of anesthesia was performed with 1–2 mg/kg of propofol, 2 μg/kg of fentanyl and 0.5 mg/kg of atracurium. After insertion of appropriately sized endotracheal tube, anesthesia was maintained with 50% O_2-air mixture, 2–3% sevoflurane and incremental doses of atracurium. Ventilation was controlled to maintain an end-tidal carbon dioxide partial pressure of 35 to 40 mmHg. No other sedatives or opioids was administered during the procedure. Quality of surgical field (QSF) was evaluated by the operating surgeon using Modena bleeding score as follows: 1 = No bleeding, 2 = Bleeding easily controlled by suctioning, washing, or packing without any significant modification or slowing of surgical procedure, 3 = Bleeding slowing surgical procedure, 4 = Most of the maneuvers dedicated to bleeding control, 5 = Bleeding that prevents every surgical procedure except those dedicated to bleeding control [13].

At end of the procedure neuromuscular blockade was reversed with IV neostigmine 0.05 mg/kg and atropine 0.02 mg/kg. Recovery time from discontinuation of anesthesia until child opens his eyes and become oriented, was recorded in minutes.

The child was transferred to the PACU once the airway is maintained spontaneously. Emergence agitation (EA) was assessed in PACU using the Watcha scale [14]. 0 = Asleep, 1 = Calm, 2 = Crying, but can be consoled, 3 = Crying, but cannot be consoled, 4 = Agitated and thrashing around. Score more than two indicates the presence of EA. Patients with agitation score more than two received intravenous midazolam (0.01–0.02 mg/kg).

Adverse events such as hypotension (MABP reduction greater than 20% from baseline value) requiring fluid bolus administration, bradycardia (HR< 100 beats/minin patients 1 to 3 years old and <60 beats/min in patients older than 3 to 8 years old) requiring atropine administration, hypoxemia (SpO_2 < 90%), the occurrence of postoperative shivering and postoperative nausea and vomiting were noted.

Time of child discharge from the postoperative care unit was the endpoint of the study. The primary outcome was parental separation assessment.

3. Statistical analysis

Using PASS 11 program for sample size calculation and assuming proportion of children with PSAS score of 1 or 2 in study groups = 70% and 95%, sample size of 25 patients per group can detect the difference between 2 groups with power 80%, setting α-error at 0.05.

The collected data were coded, tabulated and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 28.0, IBM Corp., Chicago, USA, 2021. Quantitative data evaluated

Table 1. Patients' demographic data in the two studied groups.

Variables		D 3 (n = 25)	D 4 (n = 25)	p-value
Age (years)		4.3 ± 2.0	5.0 ± 2.1	0.287
Sex	Male [N (%)]	11 (44.0%)	8 (32.0%)	0.382
	Female [N (%)]	14 (56.0%)	17 (68.0%)	
Weight (kg)		13.3 ± 3.9	14.5 ± 4.1	0.292
ASA ps	Class I [N (%)]	7 (28.0%)	5 (20.0%)	0.508
	Class II [N (%)]	18 (72.0%)	20 (80.0%)	

Data were expressed by either mean ± SD or Number (%).
n = The number of patients in each group.
N = The number of patients in each corresponding parameter.
P ≥ 0.05 = non-significant difference.
ASA ps: American society of anesthesiologist physical status.

for normality using Shapiro-Wilk test, then if normally distributed described as mean± SD (standard deviation) and compared using independent t-test. Qualitative data described as number and percentage and compared using Chi square test and Fisher's Exact test for variables with small, expected numbers. The level of significance was taken at P value < 0.05.

4. Results

Fifty pediatric patients were allocated into two equal groups. The patients in the two groups were comparable regarding their demographic characteristics (Table 1).

As regards the hemodynamic parameters, SpO_2 of both groups was comparable. The HR at 20 min and 30 min after dexmedetomidine administration and immediately after induction of GA were significantly lower in D4 than in D3 group and the rate of bradycardia was significantly higher in D4 group than in D3 group (Table 2). The MAP level immediately after induction of GA and the minimum level of MAP were significantly lower in D4 group than in D3 group and the rate of hypotension was significantly higher in D4 group than in D3 group (Table 2).

For the sedation variables, there was deeper sedation among D4 group compared to D3 group, yet the difference was statistically non-significant. The onset of sedation and the time to maximum sedative effect statistically were significantly earlier among D4 group. BIS score at admission to operating theater was statistically significantly lower among D4 group compared to D3 group. The PSAS, EVP and EA were comparable among the two groups (Table 3).

Concerning the operative characteristics, the surgical duration and the recovery time were statistically significantly shorter among D4 group compared to D3 group. QSF grades were statistically non-significantly lower among D4 group compared to D3 group (Table 4).

Table 2. Peripheral oxygen saturation, heart rate and mean pressure at various times of measurements in the two studied groups.

Time	D 3 (n = 25)	D 4 (n = 25)	p-value
	SpO_2 (%)		
Baseline	97.1 ± 1.4	96.8 ± 1.3	0.404
Minute-10	96.9 ± 1.2	96.9 ± 1.4	0.911
Minute-20	96.8 ± 1.1	96.7 ± 1.1	0.900
Minute-30	97.0 ± 1.3	96.7 ± 1.2	0.365
Induction	97.7 ± 0.7	97.7 ± 1.1	0.875
Minimum	95.8 ± 0.8	95.6 ± 0.8	0.283
Maximum	98.3 ± 0.8	98.5 ± 0.6	0.315
	Heart rate (beat/minute)		
Baseline	98.7 ± 19.7	98.0 ± 22.2	0.902
Minute-10	97.6 ± 20.0	86.2 ± 23.8	0.072
Minute-20	95.6 ± 19.6	80.9 ± 21.9	0.016*
Minute-30	93.5 ± 20.0	79.3 ± 21.2	0.019*
Induction	92.2 ± 20.4	78.8 ± 20.9	0.026*
Minimum	92.2 ± 20.4	78.8 ± 20.9	0.026*
Maximum	98.7 ± 19.7	98.0 ± 22.2	0.902
Bradycardia	0 (0.0%)	6 (24.0%)	0.022*
	Mean blood pressure (mmHg)		
Baseline	73.6 ± 10.1	76.4 ± 12.7	0.392
Minute-10	70.1 ± 10.0	69.3 ± 12.9	0.817
Minute-20	68.3 ± 9.7	65.2 ± 12.3	0.329
Minute-30	67.9 ± 9.3	62.7 ± 11.9	0.091
Induction	66.9 ± 9.4	60.6 ± 11.4	0.039*
Minimum	66.9 ± 9.4	60.6 ± 11.4	0.039*
Maximum	73.6 ± 10.1	76.4 ± 12.7	0.392
Hypotension	1 (4.0%)	7 (28.0%)	0.049*

Data were expressed by either mean ± SD or Number (%).
n = The number of patients in each group.
P ≥ 0.05 = non-significant difference. P < 0.05 = significant difference.

Table 3. Sedation levels at various times of measurements in the two studied groups.

Scales		D 3 (n = 25)	D 4 (n = 25)	p-value
		Sedation score		
Baseline	IV	10 (40.0%)	9 (36.0%)	0.771
	V	15 (60.0%)	16 (64.0%)	
Minute-10	II	3 (12.0%)	7 (28.0%)	0.346
	III	11 (44.0%)	10 (40.0%)	
	IV	11 (44.0%)	8 (32.0%)	
Minute-20	I	1 (4.0%)	5 (20.0%)	0.197
	II	15 (60.0%)	15 (60.0%)	
	III	9 (36.0%)	5 (20.0%)	
Minute-30	I	4 (16.0%)	8 (32.0%)	0.149
	II	18 (72.0%)	17 (68.0%)	
	III	3 (12.0%)	0 (0.0%)	
Onset (minutes),		10.8 ± 4.6	7.3 ± 3.9	0.006*
Peak (minutes),		20.9 ± 6.3	16.4 ± 4.9	0.007*
		Other sedation scales		
BIS		66.0 ± 2.1	63.7 ± 2.2	<0.001*
PSAS	1	10 (40.0%)	16 (64.0%)	0.142
	2	13 (52.0%)	9 (36.0%)	
	3	2 (8.0%)	0 (0.0%)	
EVP	Excellent	7 (28.0%)	13 (52.0%)	0.198
	Good	15 (60.0%)	11 (44.0%)	
	Fair	3 (12.0%)	1 (4.0%)	
EA	1	9 (36.0%)	15 (60.0%)	0.156
	2	15 (60.0%)	10 (40.0%)	
	3	1 (4.0%)	0 (0.0%)	

Data were expressed by either mean ± SD or Number (%).
n = The number of patients in each group.
BIS; Bispectral index, PSAS: parental separation anxiety scale,
EVP: Ease of venipuncture, and EA: Emergence agitation.
P ≥ 0.05 = non-significant difference.
P < 0.05 = significant difference.

Table 4. The Quality of surgical field score, surgical duration and recovery time in the two studied groups.

Variables		D 3 (n = 25)	D 4 (n = 25)	p-value
QSF	1	8 (32.0%)	14 (56.0%)	0.100
	2	10 (40.0%)	9 (36.0%)	
	3	7 (28.0%)	2 (8.0%)	
Surgical duration (minutes)		120.8 ± 6.0	113.0 ± 4.3	<0.001
Recovery time (minutes)		11.1 ± 1.3	9.2 ± 1.6	9.2 ± 1.6

Data were expressed by either mean ± SD or Number (%).
n = The number of patients in each group.
QSF = Quality of surgical field.
P ≥ 0.05 = non-significant difference.
P < 0.05 = significant difference

As to the adverse events, bradycardia and hypotension were significantly more frequent among D4 group compared to D3 group (Table 2). Episodes of desaturation, nausea and vomiting and Shivering were not recorded in either group.

5. Discussion

In the present study, Nebulized dexmedetomidine at dose four μg/kg was associated with deeper sedation, earlier onset, rapid peak sedation, better quality of surgical field and shorter recovery time compared to dose three μgm/kg. However, the higher dose did not affect the challenges that sedation can manage, as well as bradycardia and hypotension incidents were more frequent.

The anesthetic plan plays a crucial role in success of cochlear implant surgery. Smooth induction, stable hemodynamics, and bloodless surgical field without interfering with stimulation of cochlear implants are the keystone [15]. Preoperatively, deaf children require special attention; the patient's ability to express and communicate is compromised in addition the child separation from his family may be hard. Accordingly, the child suffers from remarkable confusion, anxiety, irritability, and aggression leading to sympathetic activation, hemodynamic compromise, and delayed gastric emptying leading to nausea, vomiting. All these factors accentuate the challenge of anesthetic management for pediatric cochlear implantation [16]. Surprisingly, little data about the anesthetic considerations especially sedative premedication for the management of the deaf children is available.

Dexmedetomidine, a highly selective α-2 receptor agonist with potent sedative and analgesic properties with minimal respiratory depressant effect. Also, it attenuates hemodynamic stress response to intubation enhancing smooth induction. Dexmedetomidine also significantly reduces pediatric emergence agitation after sevoflurane anesthesia. In addition, it has opioid sparing effect and reduce inhaled anesthetic requirements [5]. However, dexmedetomidine can conduct hemodynamic compromise that is predictable and dose dependent. Consequently, this hemodynamic factor accentuates the need for identifying the lowest dose to provide therapeutic effects.

Nebulized dexmedetomidine is an attractive needle-free route where intravenous access could be delayed until sedation is achieved [5]. Nebulized administration allows better distribution of the aerosol particles and augments the surface area coverage with a thin layer of drug [17]. Dexmedetomidine is a highly lipophilic drug with extensive tissue distribution. In addition, Nebulized administration as well permits rapid drug absorption that provides a bioavailability of 65% through the nasal mucosa and 82% through the buccal mucosa [18].

In the present study, we selected the dose as three μg/kg based on previous clinical study [19] that proved the clinical effectiveness of this dose in pediatrics. Previous studies have used four μg/kg by IV, IM and intranasal route safely [6,7,20]. Since the present study represents the first study investigating the preoperative sedation in deaf children, we hypothesized that nebulized dexmedetomidine would be required in the same or higher doses compared to the remaining population.

The margin of safety with nebulized dosing is presently unknown and requires further evaluation of the plasma concentrations and sedative effects of nebulized dexmedetomidine at different doses and in different populations. Plasma concentrations between 0.2 and 0.3 ng/mL result in significant and rousable sedation, whereas unarousable deep sedation occurs at plasma concentrations above 1.9 ng/ml [5]. Additionally, plasma concentrations up to 2.4 ng/mL provide minimal respiratory depression [5]. A potential limitation to the present study is that the concentration of dexmedetomidine in plasma was not measured.

Previous studies have investigated nebulized dexmedetomidine administration in variable doses. Nebulized dexmedetomidine at 1 μg/kg attenuated the increase in HR but not SBP following laryngoscopy and reduced the intraoperative anesthetic and analgesic consumption in adult patients [21]. On applying nebulized dexmedetomidine at 2 μg/kg, the hemodynamic parameters were stable with no incidence of bradycardia or hypotension [22–24]. Though, Zanaty and El Metainy found that two patients (10%) developed significant postoperative hypotension and bradycardia [8]. Anupriya and Kurhekar found that nebulized dexmedetomidine in a dose of 3 μg/kg offers stable hemodynamic parameters and only one patient (3%) developed bradycardia and four patients (13.3%) developed hypotension while nebulized dexmedetomidine in a dose of 2 μg/kg promoted no cases of bradycardia and only three patients (10.3%) developed hypotension [19].

This is consistent with the results of the present study, there was no incidence of bradycardia and only one patient (4%) developed hypotension with three μg/kg of nebulized dexmedetomidine on the other hand six patients (24%) developed bradycardia and seven patient (28%) developed hypotension with four μg/kg.

The depth of sedation requires vigilant assessment. Sedation scales rely on subjective physician's assessment. The choice of scoring system to assess the sedation level is challenging and limited in deaf children. The response to verbal stimuli as an element to assess the depth of sedation in any sedation score hinder its use in deaf children. Sedation scale (SS-5) possesses the advantage of providing the flexibility to use either verbal or tactile stimuli along with multiple studies have utilized it to assess the sedation level [11,25]. In one study, nebulized dexmedetomidine, two μg/kg, produced sedation scores at 30 min after premedication ranging between alert and calm [22]. In another study, nebulized dexmedetomidine alone at dose 2 μg/kg produced less satisfactory sedation level in comparison to combination of low dose ketamine and dexmedetomidine at dose 1 mg/kg + 1 μg/kg [8].

BIS monitors provide an objective, quantitative measurement of the level of hypnosis without the need to stimulate the patient, which encourage its use in patients with communication challenges [26]. Further, there is correlation between BIS values in moderate sedation with standard sedation scales in pediatric patients [27]. The combination of both BIS and sedative scales could provide different and complementary data especially with dexmedetomidine [28]. As dexmedetomidine has minimal effect with EEG patterns, consistent with stage 2 sleep [29].

The clinical effect of nebulized dexmedetomidine as a sedative premedication can be assessed by parental separation acceptance and intravenous cannula acceptance. In previous studies, nebulized dexmedetomidine at the dose of two μg/kg was effective in achieving calm parental separation in 77–93% of children [19,22,24] while it was achieved in 97% of childrenby increasing the dose to three μg/kg[19]. Whilst Intravenous cannulation acceptance was satisfactory in 69% of children [24] premedicated with two μg/kg nebulized dexmedetomidine. In another study, nebulized dexmedetomidine alone at dose 2 μg/kg produced comparable level of parental separation and ease of venipuncture in comparison to combination of low dose ketamine and dexmedetomidine at dose 1 mg/kg + 1 μg/kg [8].

The result of the present study showed that sedation score was comparable between the two doses. BIS score at admission to operating theater was lower among Dose 4 compared to 3 group (Relative risk −2.3 ± 0.6, 95% Confidence interval −3.5–-1.1) yet this difference was clinically irrelevant. The clinical effect of nebulized dexmedetomidine on parental separation acceptance and intravenous cannula acceptance supported these findings; both were comparable between the two doses.

Further, dose four μg/kg was associated with earlier onset (mean± standard error −3.5 ± 1.2 and 95% Confidence interval 1.0–5.9), and rapid peak sedation compared to dose three μg/kg (mean± standard error 4.5 ± 1.6 and 95% Confidence interval 1.3–7.7) yet the difference was also clinically irrelevant.

A bloodless surgical field is ultimate for cochlear implant surgery. A combination of physical and pharmacologic techniques can be used to minimize bleeding [15]. Intravenous dexmedetomidine is effective in reducing mean arterial blood pressure and heart rate. Hence, it has been reported that intravenous dexmedetomidine can provide dry surgical field during middle ear surgery [30,31] and cochlear implant surgery [15,32] in pediatric patients and accordingly it improved the quality of surgical field and decreased the operative time. Herein, the present study demonstrated that the quality of surgical field was comparable between the two doses. Conversely, the surgical duration was shorter among Dose 4 compared to Dose 3 group (mean± standard error 7.8 ± 1.5 and 95% Confidence interval 4.8–10.8) that can be attributed to better surgical field condition. The objective nature of the QSF score can ascribe the discrepancy between the QSF score and the operation duration. Even though this score was applied in multiple studies and the operating surgeon was the same during all the surgical operations involved in the present study.

The pharmacokinetic properties of dexmedetomidine may prolong the recovery time from anesthesia as dexmedetomidine half-life is 2–3 hours [33]. However, the finding was quite unexpected in the present study as the recovery time was shorter among Dose 4 group compared to Dose 3 group (mean and standard error 1.9 ± 0.4, 95% Confidence interval 1.0–2.7). The explanation is that single dosage of dexmedetomidine had little influence on recovery time [34]. The unique sedative properties of dexmedetomidine like natural sleep, in addition to its anesthetic-sparing effect may account for easy arousal from anesthesia [35]. Hence dexmedetomidine could have favorable influence on recovery time. The small sample size of the present study precludes assessment of the effect of different doses of nebulized dexmedetomidine as sedative premedication on recovery time and further study of the issue is still required.

Smooth emergence from anesthesia prevents dislodgment of the electrode array of the implant [36]. Intravenous dexmedetomidine have been reported to prevent pediatric EA after sevoflurane anesthesia in

various doses (0.15–2.0 µg/kg) [37]. This is consistent with the results of another study where incidence of EA was comparable between the two doses (2 and 3 µg/kg) [19] and the present study, wherein EA was comparable between 3 and 4 µg/kg.

Previous studies have reported that dexmedetomidine has a beneficial effect in decreasing postoperative nausea and vomiting [38]. The present study demonstrated that nebulized dexmedetomidine had no incidence of adverse effects including desaturation, nausea, vomiting and shivering except well-controllable bradycardia and hypotension that were significantly more frequent among dose 4 µgm/kg.

Conclusion

Premedication by each of three and four µg/kg of nebulized dexmedetomidine provides a satisfactory sedation level that facilitate parental separation and intravenous cannulation, but three µg/kg was superior because it was associated with lower frequency of side effects.

Disclosure statement

No potential conflict of interest was reported by the author(s).

References

[1] Jannu V, Mane RS, Dhorigol MG, et al. A comparison of oral midazolam and oral dexmedetomidine as premedication in pediatric anesthesia. Saudi J Anaesth. 2016;10(4):390–394.
[2] Davidson A, McKenzie I. Distress at induction: prevention and consequences. Curr Opin Anaesthesiol. 2011;24(3):301–306.
[3] Dua V, Sawant P, Bhadlikar P. Comparative evaluation of dexmedetomidine as a premedication given intranasally vs orally in children between 1 to 8 years of age undergoing minor surgical procedures. PACCJ. 2016;4(1):13–17.
[4] Bhat R, Santhosh MCB, Annigeri VM, et al. Comparison of intranasal dexmedetomidine and dexmedetomidine-ketamine for premedication in pediatric patients: a randomized double blind. Anesth Essays Res. 2016 May-Aug;10(2):349–355.
[5] Weerink MAS, Struys MMRF, Hannivoort LN, et al. Clinical pharmacokinetics and pharmacodynamics of dexmedetomidine. Clin Pharmacokinet. 2017;56(8):893–913.
[6] Mason KP, Lubisch N, Robinson F, et al. Intramuscular dexmedetomidine sedation for pediatric MRI and CT. Am J Roentgenol. 2011;197(3):720–725.
[7] Mason KP, Jerrold L. Dexmedetomidine in children: present knowledge and future applications. Anesth Analg. 2011;113(5):1129–1142.
[8] Zanaty OM, El Metainy SA. A comparative evaluation of nebulized dexmedetomidine, nebulized ketamine, and their combination as premedication for outpatient pediatric dental surgery. Anesth Analg. 2015;121(1):167–171.
[9] Peng K, Wu SR, Ji FH, et al. Premedication with dexmedetomidine in pediatric patients: a systematic review and meta-analysis. Clinics. 2014;69(11):777–786.
[10] Ferrari L, Leahy I, Staffa SJ, et al. The pediatric-specific american society of anesthesiologists physical status score: a multicenter study. Anesth Analg. 2021 1;132(3):807–817.
[11] Qiao H, Xie Z, Jia J. Pediatric premedication: a double-blind randomized trial of dexmedetomidine or ketamine alone versus a combination of dexmedetomidine and ketamine. BMC Anesthesiol. 2017;17(1):158.
[12] Dashiff C, Weaver MT. Development and testing of a scale to measure separation anxiety of parents of adolescents. J Nurs Meas. 2008;16(1):61–80.
[13] Alicandri-Ciufelli M, Pingani L, Mariano D, et al. Rating surgical field quality in endoscopic ear surgery: proposal and validation of the modena bleeding score. Eur Arch Otorhinolaryngol. 2019;276(2):383–388.
[14] Watcha MF, Ramirez-Ruiz M, White PF, et al. Perioperative effects of oral ketorolac and acetominophen in children undergoing bilateral myringotomy. Can J Anaesth. 1992;39(7):649–654.
[15] Amin SA, Elmawy MG. Optimizing surgical field during cochlear implant surgery in children: dexmedetomidine versus esmolol. Egypt J Anaesth. 2016;32(3):255–261.
[16] Bhalotra AR, Kakkar B. Anesthesia for the deaf and mute. Korean J Anesthesiol. 2017;70(6):654–655.
[17] Müller T, Cornelissen C, Dreher M. Nebulization versus standard application for topical anaesthesia during flexible bronchoscopy under moderate sedation - a randomized controlled trial. Respir Res. 2018;19(1):227.
[18] Gu W, Xu M, Lu H, et al. Nebulized dexmedetomidine-lidocaine inhalation as a premedication for flexible bronchoscopy: a randomized trial. J Thorac Dis. 2019 Nov;11(11):4663–4670.
[19] Anupriya J, Kurhekar P. Randomised comparison between the efficacy of two doses of nebulised dexmedetomidine for premedication in paediatric patients. Turk J Anaesthesiol Reanim. 2020 Aug;48(4):314–320.
[20] Tug A, Hanci A, Turk HS, et al. Comparison of two different intranasal doses of dexmedetomidine in children for magnetic resonance imaging sedation. Pediatr Drugs. 2015 Dec;17(6):479–485.
[21] Misra S, Behera BK, Mitra JK, et al. Effect of preoperative dexmedetomidine nebulization on the hemodynamic response to laryngoscopy and intubation: a randomized control trial. Korean J Anesthesiol. 2021 Apr;74(2):150–157.
[22] Abdel-Ghaffar HS, Kamal SM, El Sherif FA, et al. Comparison of nebulised dexmedetomidine, ketamine, or midazolam for premedication in preschool children undergoing bone marrow biopsy. Br J Anaesth. 2018 Aug;121(2):445–452.
[23] Shafa A, Habibzadeh M, Shetabi H, et al. Comparing the hemodynamic effects of nebulized dexmedetomidine and nebulized lidocaine in children undergoing fiberoptic bronchoscopy. J Adv Med Biomed Res. 2019 Jan;27(120):14–19.
[24] Bonagua DM, Crisostomo HC, Hernandez AGC, et al. The effect of dexmedetomidine nebulization as a premedication prior to peripheral intravenous access in pediatric patients and its effect on

separation anxiety score and acceptance to intravenous cannulation score. Pediatr Anesth Crit Care J. 2020;8(2):120–128.
[25] Jia JE, Chen JY, Hu X, et al. A randomised study of intranasal dexmedetomidine and oral ketamine for premedication in children. Anaesthesia. 2013 Sep;68(9):944–949.
[26] Nkihu MA, Chinwe OI, John OO, et al. Anaesthesia in a deaf-mute: use of the bispectral index monitor. Indian Anaesthetists' Forum. 2006;July:1–4.
[27] Coté CJ, Wilson S. American academy of pediatric dentistry, and american academy of pediatrics. guidelines for monitoring and management of pediatric patients before, during, and after sedation for diagnostic and therapeutic procedures. Pediatrics. 2019 jun;143(6):e20191000.
[28] Kasuya Y, Govinda R, Rauch S, et al. The correlation between bispectral index and observational sedation scale in volunteers sedated with dexmedetomidine and propofol. Anesth Analg. 2009 Dec;109(6):1811–1815.
[29] Mason KP, O'Mahony E, Zurakowski D, et al. Effects of dexmedetomidine sedation on the EEG in children. Paediatr Anaesth. 2009 Dec;19(12):1175–1183.
[30] Gupta K, Bansal M, Gupta PK, et al. Dexmedetomidine infusion during middle ear surgery under general anaesthesia to provide oligaemic surgical field: a prospective study. Indian J Anaesth. 2015 jan;59(1):26–30.
[31] Wu J, Han Y, Lu Y, et al. Perioperative low dose dexmedetomidine and its effect on the visibility of the surgical field for middle ear microsurgery: a randomised controlled trial. Front Pharmacol. 2022 feb;13:760916.
[32] El Saied MH, Mohamed NN, Mohamed HM, et al. Dexmedetomidine versus fentanyl in anesthesia of cochlear implantation in pediatric patients. Egypt J Anaesth. 2016;32(1):55–59.
[33] West N, Görges M, Poznikoff A, et al. Association of dexmedetomidine with recovery room and hospital discharge times: a retrospective cohort analysis. Paediatr Anaesth. 2021 Nov;31(11):1170–1178.
[34] Shukry M, Clyde MC, Kalarickal PL, et al. Does dexmedetomidine prevent emergence delirium in children after sevoflurane-based general anesthesia? Paediatr Anaesth. 2005;15(2):1098–1104.
[35] Kwon SY, Joo JD, Cheon GY, et al. In J.H.: effects of dexmedetomidine infusion on the recovery profiles of patients undergoing transurethral resection. J Korean Med Sci. 2016;31(1):125–130.
[36] Bajwa SS, Kulshrestha A. The cochlear implantation surgery: a review of anesthetic considerations and implications. Int J Health Allied Sci. 2013;2(4):225–229.
[37] Zhang Y, Wang X, Wu J, et al. Optimal dexmedetomidine dose to prevent emergence agitation under sevoflurane and remifentanil anesthesia during pediatric tonsillectomy and adenoidectomy. Front Pharmacol. 2019 Sep 10;10:1-5.
[38] Jin S, Liang DD, Chen C, et al. Dexmedetomidine prevent postoperative nausea and vomiting on patients during general anesthesia: a PRISMA-compliant meta-analysis of randomized controlled trials. Medicine (Baltimore). 2017 Jan;96(1):e5770.