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

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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.

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 FAMASUR 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/m², children with congenital syndromes or mental retardation or neurobehavioral disorders or history of allergic reactions to Dexmedetomidine.
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 saturation (SpO2) 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 dexmedetomine, 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 SpO2) 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% O2-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/min in patients 1 to 3 years old and <60 beats/min in patients older than 3 to 8 years old) requiring atropine administration, hypoxemia (SpO2 < 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)     | 4.1 ± 2.0    | 5.0 ± 2.1    | 0.287   |
| Sex Male [N (%)]|              |              |         |
| Male            | 11 (44.0%)   | 8 (32.0%)    |         |
| Female          | 14 (56.0%)   | 17 (68.0%)   |         |
| Weight (kg)     |              |              |         |
| 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. 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 means: SD (standard deviation) and compared using independent t-test.
Qualitative data described as number and percentage 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, SpO₂ of both groups was comparable. The HR was 70.1 ± 10.0 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 injection 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 |
|------------|--------------|--------------|---------|
| SpO₂ (%)   |              |              |         |
| 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 (beats/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), Peak (minutes), Other sedation scales | 10.8 ± 4.6 | 7.3 ± 3.9 | 0.006* |
|             | 20.9 ± 6.3  | 16.4 ± 4.9  | 0.007*  |

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                       |              |              | 0.100   |
| 1                         | 8 (32.0%)    | 14 (56.0%)   |         |
| 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    |         |

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 μg/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 children by 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 $-2.3 \pm 0.6$, 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 $-3.5 \pm 1.2$ and 95% Confidence interval 1.0–5.9), and rapid peak sedation compared to dose three μg/kg (mean: standard error $4.5 \pm 1.6$ 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 μg/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).

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