Nasal and Intravenous Administration of Dexmedetomidine to Prevent the Emergence Agitation After the Vascular Interventional Surgery in Children: A Randomized, Double-blind, Controlled Study

Huang Lei
  Kunming Children's hospital

Liu Shen Ling
  Kunming Children's hospital

Pu Yanying
  Kunming Children's Hospital

Peng Xiao Han
  Kunming Children's hospital

Xu Yun Bo
  Kunming Children's hospital

Tan Xin
  Kunming Children's hospital

Li Chao
  Kunming Children's Hospital

Li Yajun
  Kunming Children's hospital

Tan Miao (✉ 65255106@qq.com)
  Second Affiliated Hospital of Kunming Medical University

Research article

Keywords: dexmedetomidine, emergence agitation, intravenous, intranasal, pediatric

DOI: https://doi.org/10.21203/rs.3.rs-37108/v1

License: ©  This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Introduction: Dexmedetomidine reduces the incidences of postanesthetic restlessness and hemodynamic fluctuations in children within acceptable ranges. Dexmedetomidine nasal drop prior to the surgery reduces the EA after anesthesia. There are several studies that compare the effects of dexmedetomidine nasal drop and intravenous injection, in which they were administered prior to the induction of anesthesia. This double-blind, randomized, controlled study was performed to compare the effects of dexmedetomidine nasal drop and intravenous injection on postoperative emergence agitation (EA), sedation, and hemodynamics in pediatric patients prior to and post surgery.

METHODS: We randomly divided 120 children, who were enrolled in this study, into the control, dexmedetomidine nasal, and dexmedetomidine intravenous injection groups. The dexmedetomidine dose for nasal use was 2 µg / kg, and that for intravenous injection was 0.8 µg / kg. The nasal dose and the intravenous injection were, respectively, administered 30 and 10 min prior to the surgery being culminated. The EA was recorded within 30 min in the post-anesthesia care unit (PACU) and within 3 h in the ward. The incidence of EA, Ramsay scores, heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP), and adverse events were recorded.

RESULTS: In the PACU, the EA incidences in the nasal dose, intravenous injection, and control groups were 27.50%, 20.00%, and 52.50%, respectively. Statistical differences between the nasal and control groups (p < 0.05, OR = 0.343, 95% CI [0.135–0.871]) and the intravenous and control groups (p < 0.05, OR = 0.226, 95% CI [0.084–0.610]) were recorded. The EA incidence was not statistically different between the nasal and intravenous injection groups. The proportions of Propofol users were 52.50%, 27.50%, and 92.50% in the nasal spray, intravenous injection, and control groups, respectively. Statistically significant differences among the three groups (p < 0.05) were observed. The EA incidences in the nasal drop, intravenous injection, and control groups in the ward were 20.00%, 17.50%, and 70.00%, respectively. Statistically significant difference between the nasal drop and control groups (p < 0.05, OR = 0.107, 95% CI [0.038–0.300]) and the intravenous and control groups (p < 0.05, OR = 0.091, 95% CI [0.032–0.262]) were found. There was no significant difference in EA incidence between the nasal drop and intravenous injection groups.

CONCLUSION: Dexmedetomidine nasal and intravenous administrations have similar effects in reducing the EA incidence within 30 min in the PACU and 3 h in the ward. In the PACU the sedation depth in the intravenous injection group was greater than that in the nasal drop group and within the 3 h in the ward, the depth of sedation was the same for both administration routes. The intravenous injection affects the HR more than the nasal drop within 5 min of administration. Thus, dexmedetomidine nasal drop prior to the culmination of the surgery is more suitable for PACU and ward sedation to prevent EA.

Trial registration: The registration number, ChiCTR1900021325(http://www.chictr.org.cn/index.aspx), The date of registration, 02/15/2019.
Introduction

In 1961, Eckenhoff et al. first documented the emergence agitation (EA) in pediatric anesthesia [1]. The incidence of postanesthetic restlessness in pediatric patients was higher than that in adult patients (12–13% vs. 5.3%) [2], which although can generally heal by itself [3], is also reported in 2 days after surgery [4].

Dexmedetomidine is a highly selective $\alpha_2$ receptor agonist. Owing to its weak effect on respiratory depression, it is commonly used for perioperative sedation and sedation during different diagnostic tests. Dexmedetomidine is also used to prevent and treat postanesthetic restlessness [5, 6]. Hauber et al. have established through their study that a rapid intravenous injection of dexmedetomidine reduces the incidences of postanesthetic restlessness and hemodynamic fluctuations in children within acceptable ranges [7]. Dexmedetomidine nasal drop used 45 min prior to the surgery reduces the EA after anesthesia [8, 9]. There are several studies that compare the effects of dexmedetomidine nasal drop and intravenous injection [10, 11], in which they were administered prior to the induction of anesthesia. However, there were no studies that confirmed that the different routes of dexmedetomidine administration before the end of surgery have varying effects on postoperative restlessness, sedation, and hemodynamics in resuscitation rooms and wards. Patients undergoing vascular interventional diagnosis and treatment have to remain supine for a while postoperatively. During this period, the patient has to be restless in order to undergo compression hemostasis.

This double-blind, randomized, controlled study was designed to compare the effects of dexmedetomidine nasal drop and intravenous injection on postoperative restlessness, sedation, and hemodynamics in pediatric patients prior to and post surgery.

Method

1. Ethics

The Medical Ethics Committee of Kunming Children’s Hospital (No. 20181112) reviewed and approved the study, and registered it in the Chinese Clinical Trial Registry (http://www.chictr.org.cn/index.aspx) bearing the registration number ChiCTR1900021325. The consents were obtained from the participants’ guardians.

2. Sample size calculation

As per the study, the incidences of postoperative EA in children with and without dexmedetomidine were recorded to be 30% and 61%, respectively, and the difference between the two is 31% [7]. As $\alpha$ (bilateral) = 0.05; $1 - \beta = 0.8$, and the withdrawal rate is 20%, each group is determined to have 40 cases.

3. Participants
The study was performed at the Sedative and Analgesia Center of Kunming Children's Hospital between September 2018 and September 2019, and involved 120 participants in total. As per the inclusion criteria, the children, who were enrolled in the study, were of 2–10 years old, ASA I–III, and were undergoing angiography or interventional surgery. The exclusion criteria involved children who were allergic to test medications, and with severe developmental delay, maxillofacial or airway deformity, and upper respiratory infection.

4. Procedures

The enrolled patients were randomly divided into the control, dexmedetomidine nasal drip, and dexmedetomidine intravenous infusion groups using MS Excel. The dexmedetomidine stock solution (100 μg: 1 ml, Ibenin, Jiangsu Hengrui) was prepared in 1 ml syringes and the dexmedetomidine dose for the nasal drop was set as 2 μg / kg [8]. The bioavailability of dexmedetomidine for nasal drop was 40.7% [12]. Also, 2 μg / kg of nasal drop is equivalent to the intravenous infusion of 0.8 μg / kg. Thus, the dose of dexmedetomidine for intravenous injection was fixed as 0.8 μg / kg. The syringes only had number labels on them, without any difference in appearance. A nurse anesthetist completed the grouping and medicine dose preparation.

As per the ASA standard guidelines, the patients fasted prior to the surgery and were not administered any preoperative medication. The patients’ ECG, noninvasive blood pressure, and pulse oxygen saturation were monitored in the operative room. The induction of patients with venous access was performed by the administration of 2–3 μg / kg of Propofol and 0.1–0.2 μg / kg of sufentanil. For the patients without venous access, venipuncture was carried out using 8% sevoflurane and 5 L/min oxygen. For the induction, 2 mg / kg of Propofol and 0.1–0.2 μg / kg of sufentanil were used. A suitable laryngeal mask was used for each patient based on their weight. The ventilation was set at pressure control mode and the pressure was set as per the exhaled carbon dioxide partial pressure maintained at 35–45 mmHg. The concentration of sevoflurane was retained at 2%–3% during the surgery, whereas sufentanil of 0.5 μg / kg and Propofol of 1 mg / kg were added once an hour.

At 30 min prior to the culmination of the surgery, patients in the control and intravenous injection groups were each administered 1 ml saline by nasal drop. The nasal group patients were administered dexmedetomidine 2 μg / kg in 1 ml nasally. The patients of control and nasal groups were each administered 10 ml saline by intravenous injection, 10 min prior to the end of the surgery. The intravenous injection group patients were administered dexmedetomidine 0.8 μg / kg in 10 ml by intravenous injection. The anesthesiologists, who were oblivious to the group condition, administered all the intravenous injections at a slow pace to last for more than 2 min [13].

5. Assessment

Postoperatively, all the patients were shifted to the post-anesthesia care unit (PACU) with the laryngeal mask on. The heart rate (HR), blood pressure, and oxygen saturation values were recorded at 10, 20, and 30 min in the PACU. The nurse anesthetist evaluated and documented the Ramsay sedation scores in the
PACU. Pediatric Anesthesia Emergence Delirium (PAED) scale was used to assess EA once the child woke up [14]. When the restlessness of the patient affected the compression of the puncture point, 1 mg / kg of Propofol was administered to stop the bleeding, and the dosage and frequency of Propofol were recorded. On meeting the following conditions, the patients were transferred to the ward for constant monitoring: Awake and compatible or Ramsay score ≤ 4 points and Aldrete's score ≥ 8 points.

Ramsay scores were documented for the first three consecutive hours. The dosage and frequency of phenobarbital were recorded. Adverse events, such as hypoxemia, laryngospasm, vomiting, and bleeding at the puncture site, were noted. Hypoxemia is defined as pulse oxygen saturation <90% in the state of oxygen inhalation. The follow up was completed by another nurse, who was oblivious to the group condition.

6. Observation indexes

The main observational index of the experiment was the incidence of EA among the children in the PACU, for which the diagnostic criterion was PAED >12 [15]. The secondary observational index of the experiment was the incidence of EA recorded within 3 h of transferring the child to the ward (the diagnostic criterion was PAED >12), and the Ramsay scores observed in the PACU and during the first three consecutive hours in the ward.

7. Statistical analysis

Statistical analysis was carried out using the SPSS 23.0 software. Measurement data were expressed in terms of mean ± standard deviation (x ± s), single-factor ANOVA analysis was used, and the least significant difference method was used for pairwise comparison. Count data were compared using the χ² test; p < 0.05 was considered statistically significant.

Results

In this randomized, double-blind, controlled trial of a total of 120 children enrolled in the study, 40 patients each were registered in the nasal drop, intravenous injection, and control groups. The sociodemographic and clinical features of the patients have been presented in Table 1. There were no significant differences found in the ASA grade, HR, systolic blood pressure (SBP) and diastolic blood pressure (DBP), time duration of the surgery, and the use of anesthetics among the three groups.
In the PACU, the EA incidences in the nasal drop group, intravenous injection, and control groups were 27.50%, 20.00%, and 52.50%, respectively. Statistical differences in the EA incidences between the nasal and control groups ($p < 0.05$, OR $= 0.343$, 95% CI [0.135–0.871]), and intravenous injection and control groups ($p < 0.05$, OR $= 0.226$, 95% CI [0.084–0.610]) were recorded. There was no incidence of EA in both the nasal and the intravenous injection groups. The Ramsay scores of the three groups, at 10 min in the PACU, were 4.70 ± 1.70, 5.23 ± 0.53, and 3.88 ± 2.03, respectively, and there was a statistically significant difference in Ramsay scores among the three groups ($p < 0.05$). There were statistically significant differences in the Ramsay scores between the intravenous and control groups at 20 min in the PACU ($p < 0.05$). However, there were no statistical differences in the Ramsay scores among the three groups at 30 min in the PACU. The proportions of Propofol users were 52.50%, 27.50%, and 92.50% in the nasal drop, intravenous injection, and control groups, respectively ($p < 0.05$).

In the ward, the EA incidences in the nasal, intravenous injection, and control groups were 20.00%, 17.50%, and 70.00%, respectively. Statistical differences between the nasal drop and control groups ($p <
0.05, OR = 0.107, 95% CI [0.038–0.300]), and intravenous injection, and control groups (\(p < 0.05, \text{OR} = 0.091, 95\% \text{ CI} [0.032–0.262]\)) were recorded. There was no significant difference in the EA incidence between the nasal and intravenous injection groups. Differences in the Ramsay scores at 1 h, 2 h, and 3 h in the ward between the nasal drop and intravenous injection groups were compared with those of the control group (\(p < 0.05\)). The proportions of phenobarbital users were noted to be 12.50%, 15.50%, and 35.00% in the nasal drop, intravenous injection, and control groups, respectively. A statistically significant difference was observed in the proportions of phenobarbital users between the nasal and intravenous injection groups as compared with that of the control group (\(p < 0.05\); Table 2).
| Group    | Control group | Nasal group | Intravenous injection group | p     |
|----------|---------------|-------------|-----------------------------|-------|
|          | n = 40        | n = 40      | n = 40                      |       |
| PACU     |               |             |                             |       |
| PAED 12 (%) | 21 (52.50)   | 11 (27.50)  | 8 (20.00)                   | †0.022|
|          |               |             |                             | ‡0.002|
| Ramsay at 10 min | 3.88 ± 2.03 | 4.70 ± 1.70 | 5.23 ± 0.53                | †0.041|
|          |               |             |                             | ‡0.000|
|          |               |             |                             | *0.041|
| Ramsay at 20 min | 2.88 ± 2.11 | 4.10 ± 1.29 | 3.83 ± 1.71                | †0.003|
|          |               |             |                             | ‡      |
| Ramsay at 30 min | 4.3 ± 1.20   | 4.15 ± 1.06 | 4.2 ± 0.91                 | ‡0.05 |
| Propofol (%) | 37 (92.50)   | 21 (52.50)  | 11 (27.50)                  | †0.000|
|          |               |             |                             | ‡0.000|
|          |               |             |                             | *0.022|
| Ward     |               |             |                             |       |
| PAED 12 (%) | 28 (70.00)   | 8 (20.00)   | 7 (17.50)                   | †0.000|
|          |               |             |                             | ‡0.000|
| Ramsay at 1 h | 1.53 ± 1.11 | 3.402 ± 0.98| 3.23 ± 1.03                | †0.000|
|          |               |             |                             | ‡0.000|
| Ramsay at 2 h | 1.27 ± 0.55 | 2.85 ± 0.89 | 2.78 ± 0.89                | †0.000|
|          |               |             |                             | ‡0.000|
| Ramsay at 3 h | 1.6 ± 0.50   | 2.05 ± 0.32 | 2.03 ± 0.42                | †0.000|
|          |               |             |                             | ‡0.000|
| Phenobarbital (%) | 14 (35.00) | 5 (12.50)  | 6 (15.00)                   | †0.018|
|          |               |             |                             | ‡0.039|

The HRs of the nasal drop group patients were lower than those of the control group patients at 10 and 15 min after the nasal drop administration, and at 10 and 20 min in the PACU, and 1, 2, and 3 h in the ward. No statistical difference was found between the nasal and intravenous groups at any time, as shown in Fig. 2.
There was no statistically significant difference in the SBP values between the nasal drop and control groups at any time point. The SBP values of the nasal drop group patients were significantly different from those of the intravenous group (100.38 ± 6.61 vs. 104.23 ± 7.22, p < 0.05). The SBP values of the intravenous group were statistically different from those of the control group at 1 and 2 min following the intravenous injection (p < 0.05; Fig. 3). The DBP values of the nasal group were not significantly different from those of the control group at any time. A statistically significant difference between the nasal drop and intravenous groups at 1 h in the ward (52.38 ± 6.65 vs. 52.73 ± 5.53, p < 0.05) was recorded. The difference in the DBP values in the intravenous group and the control group was statistically significant at 1 min following the intravenous injection (p < 0.05; Fig. 4).

**Incidence Of Adverse Effects In Three Groups**

A case of vomiting and one with slight bleeding from the puncture point dressing, both occurred within 2 h in the ward in the absence of any drug intervention. In the intravenous group, one patient exhibited hypoxia in the PACU. Following the intravenous injection of Propofol, the patient suffered respiratory depression and the oxygen saturation declined to 86%. The patient recovered with the uplifting of the mandibular jaw for 15 s. Two other patients of the control group developed hypoxia in the PACU owing to respiratory depression caused by Propofol. The oxygen saturation declined to a value < 90% within 15 s, and was recovered on lifting the mandible. Two patients experienced slight bleeding from the puncture point dressing within 3 h in the ward, in the absence of any intervention. There were no serious adverse events or deaths.

**Discussion**

This single-center, randomized, double-blind, controlled trial showed that in children undergoing vascular interventional surgery, dexmedetomidine administered both nasally and intravenously had similar effect in lowering the EA incidence in the PACU and during the first three hours in the ward as compared with the control group. In the PACU, the sedation depth of the intravenous injection group was greater than that in the nasal drop group. Thus, the use of Propofol in the intravenous injection group was recorded to be lesser in the PACU. However, the sedation depths of the two administration routes were found to be the same within 3 h in the ward, which lowered phenobarbital usage, while the effect of intravenous administration of dexmedetomidine on the HR within 5 min was much more significant than that of the nasal group. Dexmedetomidine nasal route was found to be much more suitable for sedation and prevention of EA in the PACU and the ward than the intravenous route of administration.

The EA incidence in the dexmedetomidine nasal group in the PACU was 27.5%, which was similar to the 30% incidence shown in the study by Li et al. [9]. This incidence was 3.3% higher than that found in the study by Yao et al. [8]. In this study, the EA incidence in dexmedetomidine intravenous injection group patients in the PACU was 20%, which was lower than the findings of a study by Hauber et al. [7]. The possible reason could be the different doses used. The intravenous injection dose used in this study was
0.8 µg / kg, whereas that in Hauber's study was 0.5 µg / kg, and in the study by Tsiotou et al., it was 16.1% [16]. The outcomes showed that both nasal and intravenous injection routes could decrease the EA incidence, and the effects of the nasal drop and intravenous injection were found to be similar. The effect lasted for 3 h in the ward.

Yet another remarkable finding of this study was that in the PACU, the sedation depth of the intravenous injection group patients was greater than that in the nasal group. The Propofol use in the intravenous injection group was observed to be lower than that of the nasal group (27.50% vs. 52.50%; p < 0.05). Within 10 min in the PACU, the sedation Ramsay scores of the intravenous injection group patients were recorded to be higher than those in the nasal group (5.23 ± 0.53 vs. 4.70 ± 1.70, p < 0.05). Within 3 h of the transfer to the ward, the phenobarbital use rate in the intravenous injection group was the same as that in the nasal group (15.0% vs. 12.50%, p > 0.05). Both routes of administration could reportedly reduce the use of adjuvant sedatives within 3 h of the ward. As per the guidelines for the management of children's vascular interventional surgery, the children must remain supine for 3 h in the PACU and the ward, without exhibiting any EA to ensure the hemostasis of the puncture point by compression. The ward nurses used phenobarbital routinely for patients who were not cooperating or restless, but the effect was not good. Since June 2018, following the use of this treatment program, the children are maintained under proper sedation for 3 h postoperatively and EA is prevented after they wake up. They cooperate by being in the supine position, while being more comfortable, which in turn reduces the burden of the ward nurse.

The fluctuations in the HR, SBP, and DBP values in the patients of the nasal drops group were not observed to exceed 15% of the baseline value at any point in time, which was identical to the findings of the study by Yao et al. Another study showed that the HR and SBP fluctuations with dexmedetomidine 2 µg / kg nasal use were within 17.5% and 16.1% [8]. Based on the outcomes of the study by Lei et al., bradycardia and blood pressure values of all the children in the 9986 cases with dexmedetomidine sedation were within the normal range [17], demonstrating that the effect of dexmedetomidine nasal use on the hemodynamics was insignificant. Compared with the baseline value, the HRs in the intravenous group patients decreased most significantly at 1 min to 26.52% (79.3 ± 14.08 vs. 107.92 ± 14.91; p < 0.05), and rose to 12.11% (94.85 ± 8.83 vs.) at 5 min, which is similar to the outcomes of the study by Jooste [18]. It rose to 10.32% (96.78 ± 11.07 vs. 107.92 ± 14.91; p < 0.05) of the basic value at 30 min in the PACU, which agrees with that of Hauber's findings [7]. The study shows that the HR in the PACU was still lower than the basic value (94 ± 13 vs. 120 ± 16; p < 0.05).

None of the intravenous injection group patients were administered any medication for the reduced HR, which agreed with Mason's findings [19]. Unless the patients exhibit severe clinical symptoms or basic bradycardia, immediate intervention is not required. The study carries no evidence of the duration of the effect of dexmedetomidine on HR. This study found that the HR of children in the intravenous group returned to the basic value only after 3 h in the ward (103.01 ± 13.37 vs. 107.92 ± 14.91; p > 0.05).

However, within 3 h in the PACU and the ward, the HR of patients of the intravenous group did not exceed 15% of the baseline value. The SBP values in the intravenous injection group patients were different from the findings in the study of Mason et al. [20]. In the study, the SBP values of the intravenous injection
group patients did not demonstrate a transient increase in blood pressure. Compared with the basic value, the SBP values of the intravenous injection group patients at 1 min were not different (95.08 ± 6.13 vs. 97.7 ± 8.92; \( p > 0.05 \)). Except for the slight increase in the intravenous injection group patients at 4 and 5 min, there was no difference between the SBP and basal values at any other point of time. The DBP values of the intravenous injection group patients compared with the basic value at any point of time showed that the fluctuation direction of the DBP values was within 15%, suggesting that the effect of the intravenous injection on the DBP was insignificant.

Limitations

Certain limitations of this study are detailed in the following. First, calculating the equivalent dose of the intravenous injection and nasal drop in this study was carried out on the basis of the bioavailability of 40.7% [10] in the literature. The amount is 1.3 µg on the basis of the bioavailability of 65%, which may have severer hemodynamic effects [21]. Thus, an appropriate reference bioavailability was chosen. Second, the performance of the children in the PACU and the ward makes it easy for the nurses to guess the control group. Besides, the nurses may tend to administer more sedation, in advance, to prevent restlessness, which might cause bias. Third, as per the outcomes of Li’s study [12], the onset time of dexmedetomidine nasal drop was 47.5 min, that of intravenous injection was 15 min, and the timing of our administration was 30 min prior to the culmination of the surgery. A 10-min intravenous injection may result in inconsistencies in the depth of sedation caused by the inconsistent onset time of the two drugs in the PACU.

Conclusion

To summarize, dexmedetomidine nasal and intravenous administration exhibited the same effect on reducing the EA incidence within 3 h in the PACU and the ward. In the PACU, the sedation depth of the intravenous injection group was greater than that of the nasal group, and it was the same for both the administration routes in the ward for 3 h. Considering that the intravenous injection significantly affects the HR within 5 min of administration than the nasal drop, administering dexmedetomidine nasal drop prior to the end of the surgery is more appropriate for the PACU and ward sedation in these patients than the intravenous method.

Abbreviations

EA Emergence Agitation

PACU Post-Anesthesia Care Unit

SBP Systolic Blood Pressure

DBP Diastolic Blood Pressure
Declarations

Consent for publication

Not Applicable.

Availability of data and material

All data used in this review are included in this published article.

Competing interests

Not Applicable.

Funding

No funding was obtained for this study.

Authors' contributions

LH designed the study and wrote up the first draft of the paper. LC put forward the initial concept of experiment and the guidance of study design. SLL and XHP undertook the implementation of anesthesia. YYP, YBX and XT undertook the recruitment of patients and assistance of two anesthesia practitioners to implement anesthesia. All authors read and approved the final version of the manuscript.

Acknowledgements

Not Applicable.

References

1. Eckenhoff J, Kneale D, Dripps R. The incidence and etiology of postanesthetic excitement a clinical survey. Anesthesiology. 1961;22(5):667–73.

2. Smessaert A, Schehr CA, ARTUSIO JF JR, Observations in the immediate postanaesthesia period II. Mode of recovery. BJA: British Journal of Anaesthesia, 1960. 32(4): p. 181–185.

3. Moore J, et al. Propofol and halothane versus sevoflurane in paediatric day-case surgery: induction and recovery characteristics. Br J Anaesth. 2003;90(4):461–6.

4. Holzki J, Kretz FJ. Changing aspects of sevoflurane in paediatric anaesthesia: 1975-99. Paediatric anaesthesia. 1999;9(4):283.

5. Tobias JD. Dexmedetomidine: applications in pediatric critical care and pediatric anesthesiology. Pediatric Critical Care Medicine. 2007;8(2):115–31.

6. Mason KP, Lerman J. Dexmedetomidine in children: current knowledge and future applications. Anesthesia Analgesia. 2011;113(5):1129–42.
7. Hauber JA, et al. Dexmedetomidine as a rapid bolus for treatment and prophylactic prevention of emergence agitation in anesthetized children. Anesthesia Analgesia. 2015;121(5):1308–15.

8. Yao Y, et al. Intranasal dexmedetomidine premedication reduces minimum alveolar concentration of sevoflurane for laryngeal mask airway insertion and emergence delirium in children: a prospective, randomized, double-blind, placebo-controlled trial. Pediatric Anesthesia. 2015;25(5):492–8.

9. Li L-Q, et al., Effects of different doses of intranasal dexmedetomidine on preoperative sedation and postoperative agitation in pediatric with total intravenous anesthesia undergoing adenoidectomy with or without tonsillectomy. Medicine, 2018. 97(39).

10. Niyogi S, et al. Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with dexmedetomidine: A comparison between intravenous and intranasal route. Indian journal of anaesthesia. 2019;63(11):915.

11. Han G, Yu W-w, Zhao P. A randomized study of intranasal vs. intravenous infusion of dexmedetomidine in gastroscopy. Int J Clin Pharmacol Ther. 2014;52(9):756–61.

12. Li A, et al. Pharmacokinetic and pharmacodynamic study of intranasal and intravenous dexmedetomidine. Br J Anaesth. 2018;120(5):960–8.

13. Isik B, et al. Dexmedetomidine decreases emergence agitation in pediatric patients after sevoflurane anesthesia without surgery. Pediatric Anesthesia. 2006;16(7):748–53.

14. Sikich N, Lerman J. Development and psychometric evaluation of the pediatric anesthesia emergence delirium scale. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2004;100(5):1138–45.

15. Bajwa SA, Costi D, Cyna AM. A comparison of emergence delirium scales following general anesthesia in children. Pediatric Anesthesia. 2010;20(8):704–11.

16. Tsiotou AG, et al. Dexmedetomidine for the reduction of emergence delirium in children undergoing tonsillectomy with propofol anesthesia: A double-blind, randomized study. Pediatric Anesthesia. 2018;28(7):632–8.

17. Lei H, et al., Incidence and risk factors of bradycardia in pediatric patients undergoing intranasal dexmedetomidine sedation. Acta Anaesthesiologica Scandinavica, 2019.

18. Jooste E, et al. Acute hemodynamic changes after rapid intravenous bolus dosing of dexmedetomidine in pediatric heart transplant patients undergoing routine cardiac catheterization. Anesthesia analgesia. 2010;111(6):1490.

19. Mason KP, Lönnqvist PA. Bradycardia in perspective—not all reductions in heart rate need immediate intervention. Pediatric Anesthesia. 2015;25(1):44–51.

20. Mason KP, et al. Incidence and predictors of hypertension during high-dose dexmedetomidine sedation for pediatric MRI. Pediatric Anesthesia. 2010;20(6):516–23.

21. Iirola T, et al. Bioavailability of dexmedetomidine after intranasal administration. Eur J Clin Pharmacol. 2011;67(8):825–31.
Figure 1

Ramsay scores in the three groups within 30 min in the PACU and 3 h in the ward.
Figure 2

Heart rate in the three groups at different time points.
Figure 3

SBP in the three groups at different time points.
Figure 4
DBP in the three groups at different time points.

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.

- CONSORT2010Checklist.doc