



Comparative Effects of Total Intravenous Anesthesia with Propofol and Remifentanil Versus Inhalational Sevoflurane with Dexmedetomidine on Emergence Delirium in Children Undergoing Strabismus Surgery

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Abstract

Background: Emergence delirium (ED) is common after strabismus surgery due to postoperative visual disturbance, vomiting, and pain. Total intravenous anesthesia (TIVA) has many advantages like smooth emergence from anesthesia, decreased incidence of postoperative nausea and vomiting (PONV), and postoperative analgesia.

Objectives: Our study aimed to compare the incidence of ED using inhalational sevoflurane with dexmedetomidine (DEX) versus TIVA with remifentanil.

Methods: Eighty-four patients aged 3 - 11 years scheduled for strabismus surgery under general anesthesia were randomly allocated into two groups. Patients in group I received sevoflurane and DEX (group I, n = 42), while group II patients received TIVA with propofol and remifentanil infusion (group II, n = 42). Mean arterial pressure (MAP), heart rate (HR), and pulse oximetry (SpO₂) were monitored before induction, at induction, and every 10 minutes during the surgery. In the postanesthetic care unit (PACU), pediatric anesthesia emergence delirium (PAED), face, legs, activity, cry, and consolability (FLACC), need for rescue analgesics, recovery time, level of parents' satisfaction, and PONV were recorded.

Results: Based on the results, HR and MAP significantly decreased 10 and 20 min after induction compared to baseline in group I after infusion of DEX. The incidence of PONV was significantly lower in group II than in group I, while the recovery time was significantly shorter in group I. The incidence of emergence delirium decreased in both groups.

Conclusions: The use of either total intravenous anesthesia with propofol and remifentanil or sevoflurane inhalational anesthesia with dexmedetomidine resulted in a lower incidence of emergence delirium, although dexmedetomidine resulted in hypotension, bradycardia, and PONV.

Keywords: Propofol, Dexmedetomidine, Total Intravenous Anesthesia, Emergence Delirium

1. Background

Sevoflurane anesthesia is associated with common postoperative adverse effects. It is estimated that up to 80% of children undergoing surgeries using sevoflurane can develop emergence delirium (1). Emergence delirium (ED) is more common at the pre-school age and is characterized by short-lived psychomotor agitation, alteration of child's awareness of the surrounding environment, and decreased parents' satisfaction, resulting in bad subsequent anesthetic experience (2). Emergence delirium can last 30 minutes after surgery. Although it is a self-limited

phenomenon, it needs extra nursing care to protect the child from hurting himself or touching the site of surgery (3).

Dexmedetomidine (DEX) is a highly selective α -2 receptor agonist proven to have sedative, analgesic, and anxiolytic effects with minimal respiratory depression. These effects qualify DEX to be used for controlling postoperative ED (4). Recently, DEX has started to be used in perioperative pediatric anesthesia although its sympatholytic effects and the lack of studies evaluating its pharmacological effects have limited its use (5).

Strabismus surgery is one of the most common oph-

thalmological surgeries in pediatrics. It is commonly associated with postoperative visual disturbance, which leads to an increased risk of ED (1). In addition, around 30% of children undergoing strabismus surgeries can develop postoperative vomiting and pain, which, in turn, aggravate ED. Much research demonstrated that increased preoperative anxiety is commonly associated with increased occurrence of ED (6).

The introduction of agents such as propofol and short-acting opioids like remifentanyl and midazolam has enormously changed pediatric anesthesia practice (7). Recently, total intravenous anesthesia (TIVA) has become a good substitute for inhalational anesthesia because of its multiple advantages like smooth emergence from anesthesia, decreased incidence of postoperative vomiting (POV), and postoperative analgesia (8).

2. Objectives

Our study aimed to compare the incidence of ED using inhalational sevoflurane with DEX versus TIVA with remifentanyl.

3. Methods

Following approval by the Hospital Ethics Committee of Magrabi Center, Doha, Qatar, in June 2017, 84 patients with ASA class I or II aged 3 - 11 years scheduled for strabismus surgery were enrolled in this randomized, prospective, double-blinded study from October 2018 to January 2020. Written consent was taken from participants' parents or their legal guardians. Children with physical developmental delay, pre-existing neurological disorders, history of allergy to used medications, and cardiac disorders were excluded from the current study. All patients were fasting for eight hours for food, and four hours for clear fluids before surgery.

Basic monitoring was applied, including pulse oximetry, non-invasive blood pressure, temperature probe, electrocardiogram, and inspiratory and expiratory gas concentration. No premedication was given. Anesthesia in all groups was induced using face masks with sevoflurane (8%) in oxygen. An intravenous cannula was inserted immediately after mask induction. Then, IV glycopyrrolate 5 $\mu\text{g.kg}^{-1}$ was given to all patients, followed by the insertion of laryngeal mask airway (LMA).

Subjects were randomized into one of the two groups receiving either sevoflurane and DEX (1 mcg.kg^{-1}) using syringe pumps over 10 minutes (group I, n = 42) or TIVA with propofol (4 $\text{mg.kg}^{-1} \text{h}^{-1}$) and remifentanyl infusion (0.03 $\text{mcg.kg}^{-1} \text{min}^{-1}$) and a mixture of oxygen in the air (group

II, n = 42) in a double-blinded fashion obtained by random number generation.

Mean arterial pressure (MAP), heart rate (HR), and pulse oximetry (SpO_2) were monitored just before induction as a baseline, at induction, and every 10 minutes during the surgery. Supplementary fentanyl 0.5 mcg.kg^{-1} was given intravenously if tachycardia or hypertension occurred. Furthermore, intravenous atropine 0.01 mg.kg^{-1} was given to treat bradycardia, and 10 ml.kg^{-1} normal saline solution was administered to treat hypotension. Ondansetron 0.1 mg.kg^{-1} was given as a rescue medicine for PONV. At the end of the surgery, LMA was removed while the patients were deeply anesthetized. Then, they were brought to the postanesthetic care unit (PACU).

In the PACU, children were received by a research nurse who recorded the post-anesthesia outcome variables including ED, postoperative pain, recovery time, the need for rescue analgesics, satisfaction level of parents, and PONV. The time between the arrival of the patient to the PACU and reaching an Aldrete score of ≥ 9 was defined as recovery time. The Aldrete score is a scoring system used for the clinical evaluation of patients recovering from general anesthesia. It consists of five main items (activity, circulation, consciousness, O_2 saturation, and respiration). Each item is given a score of 0 - 2 with a maximum score of 10.

We monitored the postoperative pain using the face, legs, activity, cry, and consolability scale (FLACC). Each item is given a score of 0 - 2 with a maximum score of 10. It was started once the patient was able to do a purposeful movement. Paracetamol 15 mg.kg^{-1} was given to all children for pain relief in the PACU. Then, ED was assessed using the pediatric anesthesia emergence delirium (PAED) scale, which consists of five main items (Table 1). We asked the parents to grade their levels of satisfaction with the recovery of their children from 0-10 where 0 means very dissatisfied and 10 means very satisfied.

Table 1. The Pediatric Anesthesia Emergence Delirium Scale

Item	Score
The child makes eye contact with the caregiver; The child's actions are purposeful; The child is aware of his/her surroundings	Not at all (4); Just a little (3); Quite a bit (2); Very much (1); Extremely (0)
The child is restless; The child is inconsolable	Extremely (0); Very much (1); Quite a bit (2); Just a little (3); Not at all (4); Extremely (0)

3.1. Statistical Analysis

A sample size of 42 patients in each group was adequate to obtain an 80% power to detect a significance level ($P < 0.05$). The IBM SPSS program for Windows (version 25)

was used to do statistical analysis. Continuous variables were presented as mean and standard deviation (SD) and analysis was done using student's t-test. We used the Mann-Whitney U test for comparison between non-normally distributed variables. On the other hand, we used the chi-square test to compare qualitative data. We considered P values of less than 0.05 in any test as statistically significant.

4. Results

Of 98 children who were initially enrolled in this study, 84 children were included in the final study. No significant differences were found between the groups regarding age, sex, weight, ASA class, anesthesia duration, and surgical duration (Table 2).

Parents' satisfaction was not statistically different; 39 parents were satisfied in group I versus 37 in group II. The PAED score showed no significant difference between both groups where five out of 42 patients (12%) in group I had a score more than 10, and seven out of 42 patients (17%) had the same score in group II. Recovery time in group I (28.3 ± 5.0 min) was significantly shorter than the time in group II (40.1 ± 6.1 min). Besides, PONV was significantly reduced in patients receiving propofol and remifentanyl, with a total of three patients only experiencing PONV. In contrast, 14 patients in the DEX group experienced PONV. The FLACC score of pain showed no significant difference between both groups. There was no statistical difference in the use of rescue analgesic between group I (4.8%) and group II (2.4%) (Table 2).

Mean hemodynamic values decreased considerably 10 and 20 minutes after induction compared to baseline in group I after the infusion of DEX (Figure 1). However, HR and MAP in group II showed no significant difference in comparison with baseline (Figure 2). Atropine was used for the treatment of bradycardia in 14 children in group I while four patients only were treated by atropine in group II ($P < 0.05$) (Table 2).

5. Discussion

Emergence delirium and pain commonly affect children after strabismus surgeries, leading to postoperative agitation that needs extra care and additional nursing staff in the PACU to protect the child from hurting himself. Furthermore, parents' dissatisfaction and apprehensions are also considered (9). Postoperative medication that provides sedation and analgesia without producing respiratory depression is required in such surgeries.

In our study, we used PAED for evaluating postoperative ED. Its reliability and validity have been proven in

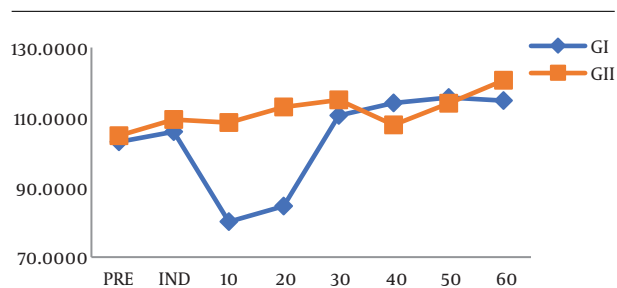


Figure 1. Intraoperative heart rate values in both groups. * $P < 0.05$ when group II is compared with group I.

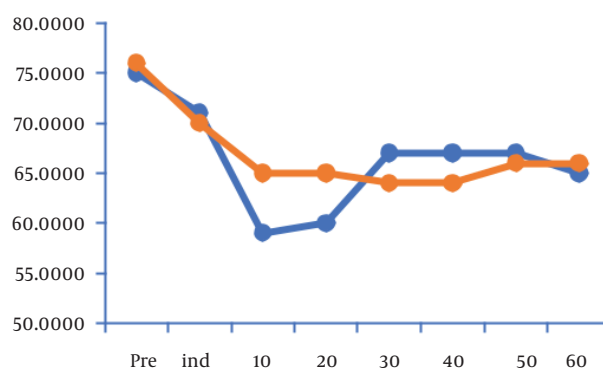


Figure 2. Intraoperative mean arterial pressure (MAP) values in both groups. * $P < 0.05$ when group II is compared with group I.

many studies (10). We found no significant difference between using sevoflurane with DEX and using propofol with remifentanyl concerning PAED. Dexmedetomidine has been used for a long time as an anxiolytic, anesthetic, analgesic, and sympatholytic agent (11). The mechanism with which it prevents postoperative ED is through the sedative effect in a way similar to natural sleep (12). In our study, TIVA using propofol plus remifentanyl resulted in a decrease in ED. Remifentanyl is an ultrashort-acting potent opioid with rapid action. Anesthesiologists are encouraged to use it as an adjunct to TIVA owing to the easiness of dose adjusting, rapid offset, and synergistic effects to propofol, leading to a decrease in its requirement (13). It is not easy to separate ED from pain-related agitation, as there is an overlap in the parameters assessing the two conditions. Therefore, the control of postoperative pain is highly recommended to reduce ED in pediatrics (14).

In our study, two children in group I and one in group II needed rescue analgesics. Olutoye et al. (15) demonstrated that administering DEX 1 mcg.kg^{-1} to children undergoing adenotonsillectomy resulted in the reduction of the dose of rescue analgesia in the PACU. These results can be ex-

Table 2. Demographic, Anesthetic, and Postanesthetic Care Unit Data ^a

	Group I (N = 42)	Group II (N = 42)	P Value
Age (y)	6.6 ± 2.5	5.8 ± 2.3	0.131
Weight (kg)	31 ± 12	29 ± 11	0.335
Sex (M/F)	25/17	20/22	0.382
ASA class I/II	33/9	36/6	0.570
Duration of anesthesia (min)	49 ± 12	47 ± 13	0.531
Parents' satisfaction ^a	39 (92.9)	37 (88.1)	0.713
Recovery time (min)	28.3 ± 5.0	40.1 ± 6.1	0.001 ^c
FLACC ^b	1 (1-3)	1 (0-4)	0.661
PAED ≥ 10	5 (11.9)	7 (16.7)	0.756
PONV	14 (33.3)	3 (7.1)	0.005 ^c
Rescue analgesic	2 (4.8)	1 (2.4)	1.0
Rescue atropine	14 (33.3)	4 (9.5)	0.015 ^c

^aValues are mean ± SD and No. (%) unless otherwise indicated.

^bMedian (interquartile range).

^cSignificant differences (P < 0.05)

plained by the analgesic effect of DEX, which is mediated by the inhibition of substance P release and activation of α -2 receptors in the dorsal horn of the spinal cord (15). Peng et al. (16) demonstrated that propofol-remifentanyl is more potent than volatile anesthesia for postoperative pain control. This finding was due to the synergism between propofol and remifentanyl caused by the inhibitory effect of propofol on NMDA receptors, which are responsible for hyperalgesia produced by remifentanyl. Amri et al. found that the intensity of pain was less in patients doing colonoscopy receiving dexmedetomidine than in other patients who received fentanyl. Dexmedetomidine resulted in a lower dose of rescue propofol when compared to the fentanyl group (17).

Our results showed a significant decrease in HR and MAP in the DEX group 10 and 20 minutes after the induction of anesthesia and 33% of children needed rescue atropine in this group. We infused DEX with loading doses over 10 min to decrease the dose-dependent biphasic, hemodynamic reaction. First, DEX increases blood pressure for a short time through the stimulation of peripheral α 2-adrenoreceptor, followed by long-lasting bradycardia and hypotension induced by central α 2-adrenoreceptor stimulation (18). This is supported by Chen et al. (19) who stated that DEX should be given as loading doses over 10 min. In their study, initial hypertension, which could happen during rapid infusion of DEX, was not noticed.

Nausea and vomiting are considered major reasons for postoperative discomfort in pediatrics. Furthermore, parents consider vomiting as the most relevant outcome

symptom postoperatively. It directly affects parents' satisfaction (20). Compared with sevoflurane, TIVA and remifentanyl reduced the risk of PONV by 26% in our study. It is now well established whether TIVA with propofol decreases the incidence of postoperative nausea and vomiting as compared to inhalational anesthesia (21). Therefore, TIVA with propofol is the anesthetic of choice for high-risk PONV patients or surgeries (7).

In conclusion, both total intravenous anesthesia using propofol and remifentanyl and inhalational anesthesia using sevoflurane in addition to dexmedetomidine had the same ED outcome but DEX was associated with a higher incidence of hypotension, bradycardia, and PONV when compared to TIVA and remifentanyl.

Footnotes

Authors' Contribution: The author was involved in the literature search, design, and editing.

Conflict of Interests: I declare that there is no conflict of interest.

Ethical Approval: Approval was obtained from the Hospital Ethics Committee of Magrabi Center, Doha, Qatar (MEEC-IRB-2018-101).

Funding/Support: I declare that this study was carried out without external funding.

Informed Consent: Written informed consent was obtained from the children's parents after being informed about the objective and procedure of our study.

References

1. Abu-Shahwan I. Effect of propofol on emergence behavior in children after sevoflurane general anesthesia. *Paediatr Anaesth*. 2008;**18**(1):55–9. doi: [10.1111/j.1460-9592.2007.02376.x](https://doi.org/10.1111/j.1460-9592.2007.02376.x). [PubMed: 18095967].
2. Sun L, Guo R, Sun L. Dexmedetomidine for preventing sevoflurane-related emergence agitation in children: a meta-analysis of randomized controlled trials. *Acta Anaesthesiol Scand*. 2014;**58**(6):642–50. doi: [10.1111/aas.12292](https://doi.org/10.1111/aas.12292). [PubMed: 24588393].
3. Vljakovic GP, Sindjelic RP. Emergence delirium in children: many questions, few answers. *Anesth Analg*. 2007;**104**(1):84–91. doi: [10.1213/01.ane.0000250914.91881.a8](https://doi.org/10.1213/01.ane.0000250914.91881.a8). [PubMed: 17179249].
4. Petroz GC, Sikich N, James M, van Dyk H, Shafer SL, Schily M, et al. A phase I, two-center study of the pharmacokinetics and pharmacodynamics of dexmedetomidine in children. *Anesthesiology*. 2006;**105**(6):1098–110. doi: [10.1097/00000542-200612000-00009](https://doi.org/10.1097/00000542-200612000-00009). [PubMed: 17122572].
5. Yao Y, Qian B, Lin Y, Wu W, Ye H, Chen Y. 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. *Paediatr Anaesth*. 2015;**25**(5):492–8. doi: [10.1111/pan.12574](https://doi.org/10.1111/pan.12574). [PubMed: 25487567].
6. Konig MW, Varughese AM, Brennen KA, Barclay S, Shackelford TM, Samuels PJ, et al. Quality of recovery from two types of general anesthesia for ambulatory dental surgery in children: a double-blind, randomized trial. *Paediatr Anaesth*. 2009;**19**(8):748–55. doi: [10.1111/j.1460-9592.2009.03054.x](https://doi.org/10.1111/j.1460-9592.2009.03054.x). [PubMed: 19538532].
7. Lauder GR. Total intravenous anesthesia will supercede inhalational anesthesia in pediatric anesthetic practice. *Paediatr Anaesth*. 2015;**25**(1):52–64. doi: [10.1111/pan.12553](https://doi.org/10.1111/pan.12553). [PubMed: 25312700].
8. Lerman J, Johr M. Inhalational anesthesia vs total intravenous anesthesia (TIVA) for pediatric anesthesia. *Paediatr Anaesth*. 2009;**19**(5):521–34. doi: [10.1111/j.1460-9592.2009.02962.x](https://doi.org/10.1111/j.1460-9592.2009.02962.x). [PubMed: 19453585].
9. Song IA, Seo KS, Oh AY, Baik JS, Kim JH, Hwang JW, et al. Dexmedetomidine injection during strabismus surgery reduces emergence agitation without increasing the oculocardiac reflex in children: A randomized controlled trial. *PLoS One*. 2016;**11**(9). e0162785. doi: [10.1371/journal.pone.0162785](https://doi.org/10.1371/journal.pone.0162785). [PubMed: 27617832]. [PubMed Central: PMC5019399].
10. Inomata S, Maeda T, Shimizu T, Satsumae T, Tanaka M. Effects of fentanyl infusion on tracheal intubation and emergence agitation in preschool children anaesthetized with sevoflurane. *Br J Anaesth*. 2010;**105**(3):361–7. doi: [10.1093/bja/aeq168](https://doi.org/10.1093/bja/aeq168). [PubMed: 20627877].
11. Mahmoud M, Mason KP. Dexmedetomidine: review, update, and future considerations of paediatric perioperative and periprocedural applications and limitations. *Br J Anaesth*. 2015;**115**(2):171–82. doi: [10.1093/bja/aev226](https://doi.org/10.1093/bja/aev226). [PubMed: 26170346].
12. Nelson LE, Lu J, Guo T, Saper CB, Franks NP, Maze M. The alpha2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. *Anesthesiology*. 2003;**98**(2):428–36. doi: [10.1097/00000542-200302000-00024](https://doi.org/10.1097/00000542-200302000-00024). [PubMed: 12552203].
13. McCormack JG. Total intravenous anaesthesia in children. *Curr Anaesth Crit Care*. 2008;**19**(5-6):309–14. doi: [10.1016/j.cacc.2008.09.005](https://doi.org/10.1016/j.cacc.2008.09.005).
14. Choi EK, Lee S, Kim WJ, Park SJ. Effects of remifentanyl maintenance during recovery on emergence delirium in children with sevoflurane anesthesia. *Paediatr Anaesth*. 2018;**28**(8):739–44. doi: [10.1111/pan.13446](https://doi.org/10.1111/pan.13446). [PubMed: 30004624].
15. Olutoye OA, Glover CD, Diefenderfer JW, McGilberry M, Wyatt MM, Larrier DR, et al. The effect of intraoperative dexmedetomidine on postoperative analgesia and sedation in pediatric patients undergoing tonsillectomy and adenoidectomy. *Anesth Analg*. 2010;**111**(2):490–5. doi: [10.1213/ANE.0b013e3181e33429](https://doi.org/10.1213/ANE.0b013e3181e33429). [PubMed: 20610555].
16. Peng K, Liu HY, Wu SR, Liu H, Zhang ZC, Ji FH. Does propofol anesthesia lead to less postoperative pain compared with inhalational anesthesia?: A systematic review and meta-analysis. *Anesth Analg*. 2016;**123**(4):846–58. doi: [10.1213/ANE.0000000000001504](https://doi.org/10.1213/ANE.0000000000001504). [PubMed: 27636574].
17. Amri P, Nahrini S, Hajian-Tilaki K, Hamidian M, Alipour SF, Hamidi SH, et al. Analgesic effect and hemodynamic changes due to dexmedetomidine versus fentanyl during elective colonoscopy: A double-blind randomized clinical trial. *Anesth Pain Med*. 2018;**8**(6). e81077. doi: [10.5812/aapm.81077](https://doi.org/10.5812/aapm.81077). [PubMed: 30719412]. [PubMed Central: PMC6347670].
18. Hauber JA, Davis PJ, Bendel LP, Martyn SV, McCarthy DL, Evans MC, et al. Dexmedetomidine as a rapid bolus for treatment and prophylactic prevention of emergence agitation in anesthetized children. *Anesth Analg*. 2015;**121**(5):1308–15. doi: [10.1213/ANE.0000000000000931](https://doi.org/10.1213/ANE.0000000000000931). [PubMed: 26332857].
19. Chen F, Wang C, Lu Y, Huang M, Fu Z. Efficacy of different doses of dexmedetomidine as a rapid bolus for children: a double-blind, prospective, randomized study. *BMC Anesthesiol*. 2018;**18**(1):103. doi: [10.1186/s12871-018-0562-0](https://doi.org/10.1186/s12871-018-0562-0). [PubMed: 30086709]. [PubMed Central: PMC6081880].
20. Sossai R, Johr M, Kistler W, Gerber H, Scharli AF. Postoperative vomiting in children. A persisting unsolved problem. *Eur J Pediatr Surg*. 1993;**3**(4):206–8. doi: [10.1055/s-2008-1063544](https://doi.org/10.1055/s-2008-1063544). [PubMed: 8218070].
21. Biallas R, Rusch D, de Decker W, Wulf H, Siebrecht D, Scholz J. [Prophylaxis of postoperative nausea and vomiting (PONV) in children undergoing strabismus surgery. Sevoflurane/N2O plus dimenhydrinate vs. propofol/remifentanyl plus dimenhydrinate]. *Anaesthesist*. 2003;**52**(7):586–95. German. doi: [10.1007/s00101-003-0516-9](https://doi.org/10.1007/s00101-003-0516-9). [PubMed: 12898043].