



A Comparison of the Sevoflurane and Total Intravenous Anesthesia on the Quality of Recovery in 2 to 10-Year-Old Children

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Abstract

Background: Inhalant anesthesia is one of the mainstays of pediatric anesthesia, and it is considered by the majority of pediatric anesthesiologists worldwide as the gold standard. On the other hand, total intravenous anesthesia (TIVA) is a very popular choice for routine pediatric anesthesia practice. Therefore, utilization of TIVA compared to the volatile anesthesia is still a topic of debate in successful anesthesia management.

Objectives: To compare TIVA vs sevoflurane-based anesthesia on the quality of recovery in children aged 2 to 10 years who had outpatient surgery.

Methods: Eighty children, aged 2 to 10 years old undergoing outpatient surgery, were randomly divided into two groups (40 patients each). The TIVA group with propofol (T) received general anesthesia induced with midazolam 0.03 - 0.05 mg/kg, fentanyl 1 mcg/kg, propofol 3 - 5 mg/kg, 0.1 mg/kg lidocaine and maintenance with propofol 100 to 250 μ g/kg.min and remifentanyl 0.1 mcg/kg. The sevoflurane (S) group received general anesthesia induced with midazolam 0.03 - 0.05 mg/kg, fentanyl 1 mcg/kg, O₂/sevoflurane 8 vol%, maintenance with 2 - 3 vol%. Demographic characteristics, awakening quality in recovery, hemodynamic status, and other complications such as patient agitation, pain, nausea, and vomiting were evaluated in both groups.

Results: Patients did not differ significantly in terms of demographic characteristics. The incidence of postoperative agitation was 62% higher in the sevoflurane group than the TIVA group (5%, $P < 0.001$). The highest percentage of pain was obtained as 52.5% in the sevoflurane group. Postoperative nausea and vomiting did not differ significantly among groups, and there was a significant decrease in the heart rate of the subjects in the T group as one of the hemodynamic variables ($P = 0.01$).

Conclusions: Inhalation anesthesia with sevoflurane led to more rapid recovery from anesthesia, and TIVA with propofol injection reduced post-operative pain and agitation compared to patients receiving sevoflurane. Therefore, TIVA with propofol infusion is probably an effective technique to maintain general anesthesia in pediatric outpatient surgery and to increase parental satisfaction, and to reduce the workload of recovery room staff.

Keywords: Recovery, Sevoflurane, Total Intravenous Anesthesia (TIVA), Pediatric Anesthesia

1. Background

The main goals of anesthesia for pediatric outpatient surgery are rapid emergence, short recovery with low postoperative side effects, and rapid discharge (1). Inhalation anesthesia has been the basis of pediatric anesthesia for more than 150 years due to its efficacy, reliability, safety, stability, ease of delivery, and not having end-organ consequences (2). The majority of pediatric anesthesiologists worldwide are considering it as the gold standard (3). Meanwhile, with the advances in understanding the pharmacological properties and availability of fast-acting drugs, to-

tal intravenous anesthesia (TIVA) has become an appealing option in general anesthesia in children (4-6). Therefore, utilization of TIVA compared to volatile anesthesia is still a topic of debate in successful anesthesia management.

2. Objectives

The current study aimed to compare inhalation anesthesia with sevoflurane and total intravenous anesthesia (TIVA) with propofol infusion on the quality of recovery. Secondary measures included postoperative pain, postop-

erative nausea and vomiting, hemodynamic status, and duration of post-anesthesia care unit (PACU) stay.

3. Methods

The study was conducted from March 2019 to August 2019 at Tabriz Pediatric Hospital. 80 cases aged 2 - 10 years who were scheduled to undergo herniotomy, orchiopexy, frenulectomy, and sigmoidoscopy surgery were included. Exclusion criteria included having a known allergy to any of the drugs involved in the study, being on an anticonvulsant, having purulent nasal discharge, fever, and history of malignant hyperthermia, cardiopulmonary disease, or other organic dysfunction. Patients were allowed to take solid food until 8 hours, milk products until 6 hours, and clear liquids until 3 hours before the surgery. The participating patients were randomly assigned to one of the two groups of TIVA with propofol (T) or sevoflurane (S) anesthesia using a computer-generated random number table. Routine investigations were performed in the operation room. Non-invasive monitors, such as electrocardiogram, blood pressure, oxygen saturation, and bispectral index (BIS) were attached for recording baseline parameters. To have an adequate depth of anesthesia, the BIS value was regulated between 40 and 60. The TIVA group with propofol (T) anesthesia induced with midazolam 0.03 - 0.05 mg/kg, fentanyl 1mcg/kg, propofol 3 - 5 mg/kg, 0.1 mg/kg lidocaine, and an appropriate size of laryngeal mask airway (LMA) was implanted, and the anesthesia continued with propofol infusion 100 to 250 μ g/kg/min and remifentanyl 0.1 mcg/kg. The concentration of remifentanyl was modified in accordance with the BIS. The sevoflurane (S) group received general anesthesia induced with midazolam 0.03 - 0.05 mg/kg, fentanyl 1mcg/kg, O₂/sevoflurane 8 vol%, maintenance with 2 - 3vol%. The concentration of sevoflurane was modified in accordance with the BIS, heart rate, and blood pressure. After successful extubation, children were transferred to the PACU. Demographic characteristics, awakening quality in recovery, agitation, and other complications such as pain, nausea, vomiting, and hemodynamic status were documented by an experienced nurse. Postoperative pain was equal in the two groups and was measured 15 minutes after surgery using the Wong-Baker Faces Pain Rating Scale and pain relief was provided by rectal acetaminophen. Collected data were evaluated using statistical-descriptive methods (i.e., mean, standard deviation, frequency, and percentage). The independent-samples t-test was used to compare quantitative data. The non-normal distribution of data was assessed by the Kolmogorov-Smirnov test and Chi-Square test. Data were analyzed by SPSS version 20. A P-Value of < 0.05 was considered as statistically significant.

4. Results

Of 95 children to be evaluated, 15 were excluded. The remaining 80 patients were randomly allocated to the two defined groups. 40 children were planned to receive sevoflurane, and 40 children were planned to receive propofol and remifentanyl. The characteristics of patients are presented in Table 1. Patients in the two groups were not significantly different in terms of gender, American Society of Anesthesiologists (ASA) class, and body weight. Anesthesia and surgery time were similar in both groups (Table 1). There were significant differences concerning the eye-opening time (14 and 22 minutes) and the time of staying in recovery (25 and 35 minutes), respectively, between the sevoflurane and TIVA groups ($P < 0.001$) (Table 2).

The incidence of postoperative agitation was higher in the sevoflurane group (62%) than the TIVA group (5%) ($P < 0.001$), and 30 and 17.5% of the patients had postoperative nausea and vomiting in TIVA and sevoflurane groups, respectively (Table 3). In this study, the highest percentage of pain was found in the sevoflurane group, 52.5% of the children were anesthetized with sevoflurane experienced pain compared to 25.0% of the children who were anesthetized with TIVA (Table 3). Investigating hemodynamic variables (Table 4) revealed no difference in systolic pressure, diastolic pressure, and arterial oxygen saturation during the recovery between the two groups. But there was a significant decrease in the heart rate of the patients in the T group ($P < 0.001$).

5. Discussion

Inhalation anesthesia using the sevoflurane and TIVA with propofol are two techniques that are widely used to maintain anesthesia in pediatric patients undergoing general anesthesia for outpatient surgery. However, discussions about the best anesthesia technique for children still continue among anesthetists. The results of this study showed significant differences in eye-opening time (14 and 22 minutes) and the time of staying in the recovery room (25 and 35 minutes), respectively, between sevoflurane and TIVA groups ($P < 0.001$). Time to eye-opening and recovery stay was significantly shorter in the sevoflurane group than the TIVA. McFarlan et al. (1999) argued that recovery after brief anesthesia with TIVA may be as fast as when using inhalation anesthesia. Besides, recovery after prolonged anesthesia with TIVA is likely to be much protracted than after inhalation anesthesia (7). These findings aren't in line with our study. Also, Steur et al showed that prolongation in the duration of stay in the PACU in propofol recipients is due to its oversedation, resulting in slower discharge, which is not conducive to outpatient surgery cen-

Demographics and Perioperative Characteristics of the Patients

	(T) Group, (n = 40)	(S) Group, (n = 40)	P-Value
Age (y)	6 ± 1	5 ± 2	0.537
Gender (M/F)	30/10	30/10	1.00
Weight (kg)	18.2 ± 4	15.6 ± 5	0.077
ASA (I/II)	40/0	37/3	0.98
Duration of anesthesia (min)	48 ± 10	46 ± 9	0.329
Duration of surgery (min)	36 ± 8	34 ± 9	0.209

Table 2. Information Regarding the Recovery Time

Time Intervals (Min)	(T) Group, (n = 40)	(S) Group, (n=40)	P-Value
Time to eye opening (min)	22 ± 5	14 ± 4	< 0.001 ^a
Duration of PACU stay (min)	35 ± 5	25 ± 4	< 0.001 ^a

^aP < 0.05 versus Group (T) and Group (S)

Table 3. Postoperative Adverse Events

Adverse events	Group (T), (n = 40)	Group (S), (n = 40)	P-Value
Agitation (% within)	2/40 (5.0)	25/40 (62.5)	< 0.001 ^a
Nausea or vomiting (% within)	12/40 (30.0)	7/40 (17.5)	1.00
Pain % (Score 4 - 8)	25.0%	52.5%	0.05

^aP < 0.05 versus Group (T) and Group (S).

Table 4. Comparison of Hemodynamics BP, HR, SpO₂ in the Two Groups^a

Group	Entering the Recovery	5 Min	10 Min	20 Min	Before Discharge	P-Value
SBP (mmHg)						0.132
(T)	99 ± 9	100 ± 9	102 ± 11	105 ± 9	107 ± 10	
(S)	98 ± 10	102 ± 12	103 ± 12	100 ± 12	108 ± 12	
DBP (mmHg)						0.366
(T)	56 ± 8	57 ± 8	59 ± 24	62 ± 9	63 ± 9	
(S)	55 ± 10	60 ± 13	62 ± 18	61 ± 9	59 ± 8	
HR (beats/min)						< 0.01 ^b
(T)	95.7 ± 8	97 ± 6	98 ± 7	100 ± 7	104 ± 7	
(S)	104 ± 16	105 ± 11	104 ± 7	104 ± 10	109 ± 9	
SpO₂ (mmHg)						0.832
(T)	98 ± 1	98 ± 1	99 ± 1	98 ± 0	98 ± 1	
(S)	99 ± 0	98 ± 1	98 ± 1	98 ± 1	99 ± 0	

^aValues are expressed as mean ± SD.

^bP < 0.05 versus Group (T) and Group (S).

ters (8). In this study, postoperative pain was measured by the Wong-Baker Faces Pain Rating Scale. Patients receiving sevoflurane had a higher percentage of postoperative pain than patients receiving TIVA. Many studies have suggested that propofol-based anesthesia reduces postopera-

tive pain (9-11). Hasani et al. (2013) reported that 24.3% of children anesthetized with sevoflurane experienced pain, compared to 4.5% of children anesthetized with propofol (6). Chandler et al. (2013) also found higher pain scores after administration of sevoflurane, compared to propo-

fol, in children aged between 2 and 6 years who underwent strabismus surgery and concluded that TIVA can reduce the pain scores (9). In the current study, postoperative nausea and vomiting were higher in the TIVA group but were not significantly different. Some studies have reported a higher incidence of nausea and vomiting after sevoflurane anesthesia compared to propofol anesthesia (8, 9, 12). The studies conducted by Picard et al. (2000) investigated the quality of recovery after administration of sevoflurane anesthesia, compared to propofol anesthesia for tonsillectomy in children and did not find any difference concerning the postoperative nausea and vomiting (PONV) between the two groups (1), which is consistent with the findings of the current study. Studies have also shown that propofol may have anti-inflammatory activities, even at very low doses, and is mainly effective in preventing vomiting early after the operation (13-15). Pieters et al. (2010) reported an incidence of 5.4% for the PONV among those who received propofol anesthesia compared to sevoflurane anesthesia (36.8%). Only 1 (out of 200) patients included in this study received anti-nausea in the PACU (10). The study also showed that agitation was more common in children who received sevoflurane anesthesia than in children who underwent TIVA anesthesia. Naito et al. (16) compared agitation after anesthesia with sevoflurane and halothane in children and explained the high incidence of agitation and fidget in children anesthetized with sevoflurane. Also, in one study, the most common causes of agitation are reported, including hypoxemia (decreased tissue oxygen), pain, anxiety, hypoglycemia, hyponatremia (decreased blood sodium), and residual drug effects (17). Another study has considered postoperative agitation as an abnormal and scary behavior (18). Postoperative agitation is commonly performing for preschool children after receiving inhalation anesthetic agents such as sevoflurane (19), desflurane (20), and isoflurane (21, 22). In the present study, hemodynamic parameters were evaluated, and no difference in systolic pressure, diastolic pressure, and arterial oxygen saturation was observed, but heart rate was significantly decreased in the T group ($P = 0.01$). Previous studies have reported decreased HR in the TIVA group (23, 24) and it has been argued that this is partly due to the stronger inhibition of the neuroendocrine stress response by the TIVA (25). Studies have also shown that sevoflurane has a more outstanding parasympatholytic effect than TIVA (26, 27).

5.1. Conclusion

Inhalation anesthesia with sevoflurane led to more rapid recovery from anesthesia, and TIVA with propofol injection reduced post-operative pain and agitation compared to patients receiving sevoflurane. Therefore, TIVA

with propofol infusion is probably an effective technique to maintain general anesthesia in pediatric outpatient surgery and to increase parental satisfaction, and to reduce the workload of recovery room staff.

Footnotes

Authors' Contribution: Mehdi Razaghipour Sorkhab, Daryoush SheikhZadeh. developed the original idea and the protocol, abstracted and analyzed data, wrote the manuscript, and is a guarantor. Mahin Seyedhejazi and Behzad Aliakbari Sharabiani, Marzieh Marahem. contributed to the development of the protocol, abstracted data, and prepared the manuscript.

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References

- Picard V, Dumont L, Pellegrini M. Quality of recovery in children: sevoflurane versus propofol. *Acta Anaesthesiol Scand*. 2000;**44**(3):307-10. doi: [10.1034/j.1399-6576.2000.440315.x](https://doi.org/10.1034/j.1399-6576.2000.440315.x). [PubMed: [10714845](https://pubmed.ncbi.nlm.nih.gov/10714845/)].
- 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](https://pubmed.ncbi.nlm.nih.gov/19453585/)].
- Omara AF, Abdelrahman AF, Elshiekh ML. Recovery with propofol anesthesia in children undergoing cleft palate repair compared with sevoflurane anesthesia. *Anesth Pain Med*. 2019;**9**(3). e92076. doi: [10.5812/aapm.92076](https://doi.org/10.5812/aapm.92076). [PubMed: [31497524](https://pubmed.ncbi.nlm.nih.gov/31497524/)]. [PubMed Central: [PMC6712429](https://pubmed.ncbi.nlm.nih.gov/PMC6712429/)].
- Neal KD. *Inhalation anesthesia vs. Total intravenous anesthesia for ambulatory dental surgery in children [Theses]*. Dissertations and Capstones: Marshall University; 2015.
- Scheiermann P, Herzog F, Siebenhofer A, Strametz R, Weberschock T. Intravenous versus inhalational anesthesia for pediatric inpatient surgery - A systematic review and meta-analysis. *J Clin Anesth*. 2018;**49**:19-25. doi: [10.1016/j.jclinane.2018.05.014](https://doi.org/10.1016/j.jclinane.2018.05.014). [PubMed: [29860223](https://pubmed.ncbi.nlm.nih.gov/29860223/)].
- Hasani A, Gecaj-Gashi A, Llullaku S, Jashari H. Postoperative analgesia in children after propofol versus sevoflurane anesthesia. *Pain Med*. 2013;**14**(3):442-6. doi: [10.1111/pme.12031](https://doi.org/10.1111/pme.12031). [PubMed: [23294622](https://pubmed.ncbi.nlm.nih.gov/23294622/)].
- McFarlan CS, Anderson BJ, Short TG. The use of propofol infusions in paediatric anaesthesia: a practical guide. *Paediatr Anaesth*. 1999;**9**(3):209-16. [PubMed: [10320599](https://pubmed.ncbi.nlm.nih.gov/10320599/)].
- Steur RJ, Perez RS, De Lange JJ. Dosage scheme for propofol in children under 3 years of age. *Paediatr Anaesth*. 2004;**14**(6):462-7. doi: [10.1111/j.1460-9592.2004.01238.x](https://doi.org/10.1111/j.1460-9592.2004.01238.x). [PubMed: [15153207](https://pubmed.ncbi.nlm.nih.gov/15153207/)].
- Chandler JR, Myers D, Mehta D, Whyte E, Groberman MK, Montgomery CJ, et al. Emergence delirium in children: a randomized trial to compare total intravenous anesthesia with propofol and remifentanyl to

- inhalational sevoflurane anesthesia. *Paediatr Anaesth*. 2013;**23**(4):309-15. doi: [10.1111/pan.12090](https://doi.org/10.1111/pan.12090). [PubMed: [23464658](https://pubmed.ncbi.nlm.nih.gov/23464658/)].
10. Pieters BJ, Penn E, Nicklaus P, Bruegger D, Mehta B, Weatherly R. Emergence delirium and postoperative pain in children undergoing adenotonsillectomy: a comparison of propofol vs sevoflurane anesthesia. *Paediatr Anaesth*. 2010;**20**(10):944-50. doi: [10.1111/j.1460-9592.2010.03394.x](https://doi.org/10.1111/j.1460-9592.2010.03394.x). [PubMed: [20735801](https://pubmed.ncbi.nlm.nih.gov/20735801/)].
 11. König 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](https://pubmed.ncbi.nlm.nih.gov/19538532/)].
 12. Jellish WS, Lien CA, Fontenot HJ, Hall R. The comparative effects of sevoflurane versus propofol in the induction and maintenance of anesthesia in adult patients. *Anesth Analg*. 1996;**82**(3):479-85. doi: [10.1097/00000539-199603000-00009](https://doi.org/10.1097/00000539-199603000-00009). [PubMed: [8623947](https://pubmed.ncbi.nlm.nih.gov/8623947/)].
 13. Apfel CC, Kranke P, Katz MH, Goepfert C, Papenfuss T, Rauch S, et al. Volatile anaesthetics may be the main cause of early but not delayed postoperative vomiting: a randomized controlled trial of factorial design. *Br J Anaesth*. 2002;**88**(5):659-68. doi: [10.1093/bja/88.5.659](https://doi.org/10.1093/bja/88.5.659). [PubMed: [12067003](https://pubmed.ncbi.nlm.nih.gov/12067003/)].
 14. Gan TJ, El-Molem H, Ray J, Glass PS. Patient-controlled antiemesis: a randomized, double-blind comparison of two doses of propofol versus placebo. *Anesthesiology*. 1999;**90**(6):1564-70. doi: [10.1097/00000542-199906000-00011](https://doi.org/10.1097/00000542-199906000-00011). [PubMed: [10360853](https://pubmed.ncbi.nlm.nih.gov/10360853/)].
 15. Gan TJ, Glass PS, Howell ST, Canada AT, Grant AP, Ginsberg B. Determination of plasma concentrations of propofol associated with 50% reduction in postoperative nausea. *Anesthesiology*. 1997;**87**(4):779-84. doi: [10.1097/00000542-199710000-00010](https://doi.org/10.1097/00000542-199710000-00010). [PubMed: [9357878](https://pubmed.ncbi.nlm.nih.gov/9357878/)].
 16. Naito Y, Tamai S, Shingu K, Fujimori R, Mori K. Comparison between sevoflurane and halothane for paediatric ambulatory anaesthesia. *Br J Anaesth*. 1991;**67**(4):387-9. doi: [10.1093/bja/67.4.387](https://doi.org/10.1093/bja/67.4.387). [PubMed: [1931394](https://pubmed.ncbi.nlm.nih.gov/1931394/)].
 17. Wetchler B. Problem solving in the postanesthesia care unit. *Anesthesia for ambulatory surgery*. 2nd ed. Philadelphia: JB Lippincott; 1991. p. 375-434.
 18. Eger E2, Shafer SL. Tutorial: context-sensitive decrement times for inhaled anesthetics. *Anesth Analg*. 2005;**101**(3):688-96. table of contents. doi: [10.1213/01.ANE.0000158611.15820.3D](https://doi.org/10.1213/01.ANE.0000158611.15820.3D). [PubMed: [16115976](https://pubmed.ncbi.nlm.nih.gov/16115976/)].
 19. Baum VC. The bispectral index does not correlate with clinical signs of inhalational anesthesia during sevoflurane induction and arousal in children. *Survey Anesthesiol*. 2005;**49**(1):32-3. doi: [10.1097/01.sa.0000151225.21888.f5](https://doi.org/10.1097/01.sa.0000151225.21888.f5).
 20. Ravi PR, Nanda HS, Anant S. Comparative study of recovery after sevoflurane versus halothane anaesthesia in adult patients. *Med J Armed Forces India*. 2008;**64**(4):325-8. doi: [10.1016/S0377-1237\(08\)80011-1](https://doi.org/10.1016/S0377-1237(08)80011-1). [PubMed: [27688568](https://pubmed.ncbi.nlm.nih.gov/27688568/)]. [PubMed Central: [PMC5035265](https://pubmed.ncbi.nlm.nih.gov/PMC5035265/)].
 21. Meyer RR, Munster P, Werner C, Brambrink AM. Isoflurane is associated with a similar incidence of emergence agitation/delirium as sevoflurane in young children—a randomized controlled study. *Paediatr Anaesth*. 2007;**17**(1):56-60. doi: [10.1111/j.1460-9592.2006.01998.x](https://doi.org/10.1111/j.1460-9592.2006.01998.x). [PubMed: [17184433](https://pubmed.ncbi.nlm.nih.gov/17184433/)].
 22. Bortone L, Ingelmo P, Grossi S, Grattagliano C, Bricchi C, Barantani D, et al. Emergence agitation in preschool children: double-blind, randomized, controlled trial comparing sevoflurane and isoflurane anesthesia. *Paediatr Anaesth*. 2006;**16**(11):138-43. doi: [10.1111/j.1460-9592.2006.01954.x](https://doi.org/10.1111/j.1460-9592.2006.01954.x). [PubMed: [17040302](https://pubmed.ncbi.nlm.nih.gov/17040302/)].
 23. Lodes U. [Total intravenous anesthesia (TIVA) and balanced anesthesia with short-acting anesthetics for ENT surgery in children]. *Anaesthesiol Reanim*. 1999;**24**(1):13-8. [PubMed: [10220941](https://pubmed.ncbi.nlm.nih.gov/10220941/)].
 24. Juckenhofel S, Feisel C, Schmitt HJ, Biedler A. [TIVA with propofol-remifentanyl or balanced anesthesia with sevoflurane-fentanyl in laparoscopic operations. Hemodynamics, awakening and adverse effects]. *Anaesthesist*. 1999;**48**(11):807-12. doi: [10.1007/s001010050789](https://doi.org/10.1007/s001010050789). [PubMed: [10631440](https://pubmed.ncbi.nlm.nih.gov/10631440/)].
 25. Ledowski T, Bein B, Hanss R, Paris A, Fudickar W, Scholz J, et al. Neuroendocrine stress response and heart rate variability: a comparison of total intravenous versus balanced anesthesia. *Anesth Analg*. 2005;**101**(6):1700-5. doi: [10.1213/01.ane.0000184041.32175.14](https://doi.org/10.1213/01.ane.0000184041.32175.14). [PubMed: [16301244](https://pubmed.ncbi.nlm.nih.gov/16301244/)].
 26. Wodey E, Senhadji L, Pladys P, Carre F, Ecoffey C. The relationship between expired concentration of sevoflurane and sympathovagal tone in children. *Anesth Analg*. 2003;**97**(2):377-82. table of contents. doi: [10.1213/01.ane.0000068825.96424.f3](https://doi.org/10.1213/01.ane.0000068825.96424.f3). [PubMed: [12873921](https://pubmed.ncbi.nlm.nih.gov/12873921/)]. [PubMed Central: [PMC2683252](https://pubmed.ncbi.nlm.nih.gov/PMC2683252/)].
 27. Jeong SJ, Han JI, Baik HJ, Lee H, Lee GY, Kim JH. The effect of pyridostigmine on bispectral index during recovery from sevoflurane anesthesia. *Korean J Anesthesiol*. 2011;**61**(6):460-4. doi: [10.4097/kjae.2011.61.6.460](https://doi.org/10.4097/kjae.2011.61.6.460). [PubMed: [22220221](https://pubmed.ncbi.nlm.nih.gov/22220221/)]. [PubMed Central: [PMC3249566](https://pubmed.ncbi.nlm.nih.gov/PMC3249566/)].