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ORIGINAL ARTICLE

The effects of dexmedetomidine and tramadol on post-operative pain and agitation, and extubation quality in paediatric patients undergoing adenotonsillectomy surgery: A randomized trial

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Abstract

What is known and objective: Adenotonsillectomies are common surgical procedures performed under general anaesthesia in childhood. Post-operative pain and agitation are complications associated with this procedure. We compared the effects of dexmedetomidine and tramadol on post-operative pain, agitation, haemodynamic parameters, and extubation quality in patients undergoing an adenotonsillectomy using sevoflurane as an anaesthetic agent.

Methods: Sixty paediatric patients who had undergone an adenotonsillectomy were included in this study. The patients were randomized into two groups that received either dexmedetomidine (n = 30) or tramadol (n = 30). Haemodynamic variables, extubation time, post-operative pain, agitation and adverse events were recorded for all patients. Post-operative pain was assessed with the pain point system scale (PPSS), and agitation was assessed using the Riker Sedation-Agitation Scale (SAS).

Results: Patients in the dexmedetomidine group had significantly lower heart rates than the tramadol group. In addition, patients in the dexmedetomidine group had significantly lower post-operative PPSS and Riker SAS scores than patients in the tramadol group. Not breathing, cough-bucking and desaturation after extubation occurred less frequently in patients who received dexmedetomidine than in patients who received tramadol. However, the time to extubation was significantly longer for patients who received dexmedetomidine.

What is new and conclusion: Our study demonstrated that dexmedetomidine was more effective than tramadol for mitigating post-operative pain and agitation in paediatric patients following an adenotonsillectomy with sevoflurane. Although dexmedetomidine was associated with a longer time to extubation, it was also associated with fewer complications following extubation compared with tramadol.

KEYWORDS

adenotonsillectomy, dexmedetomidine, paediatric patients, tramadol

1 | WHAT IS KNOWN AND OBJECTIVE

Adenotonsillectomies are common surgical procedures that are performed under general anaesthesia in childhood.[1] Although adenotonsillectomies are valuable procedures, post-operative pain and agitation can be unwanted by-products that are stressful for patients. In turn, stress can exacerbate patient recoveries and cause adverse events. Therefore, effective pain control is important for diminishing post-operative morbidity.[2]

Volatile anaesthetic agents commonly cause agitation in paediatric patients. Sevoflurane is the volatile agent most commonly used in children for inducing and maintaining general anaesthesia. Sevoflurane is preferred because it has a tolerable smell, induces anaesthesia quickly, results in a faster recovery and is less irritating to the airways.[3] However, its high solubility produces a higher frequency of agitation than other volatile anaesthetics.[4] Agitation is characterized by meaningless and involuntary movements, restlessness, crying, yelling, disorientation and dissonance. Agitation can increase the risk of self-injury, hospitalization times, anxiety in parents and treatment cost.[5]

Post-operative pain is another complication that occurs during recovery from general anaesthesia. It can cause decreased oral intake and dehydration.[6] Some analgesic and sedative agents can be used to prevent post-operative pain and agitation. Dexmedetomidine and tramadol are two drugs used for this purpose.

Dexmedetomidine (Precedex, Pfizer) is a selective alpha-2 agonist that has sedative, analgesic and anxiolytic properties.[7,8] It also reduces stress responses to adenotonsillectomies without causing respiratory depression. Previous studies have shown that dexmedetomidine produced a beneficial effect in paediatric patients and reduced post-operative agitation and pain.[5,9-11]

Tramadol (Contramal, Abdi Ibrahim) is an opioid derived from aminocyclohexanol. It is one of the most commonly prescribed analgesics to treat moderate to severe pain, partly because of its long duration of action, fast recovery and minimal impact on respiratory depression.[12] Reports of tramadol use in children are limited, although tramadol is associated with effective post-operative pain control.[13]

There have been few reports comparing the effects of tramadol and dexmedetomidine in paediatric patients who have undergone adenotonsillectomy surgery. Thus, we compared the effects of dexmedetomidine and tramadol on post-operative pain and agitation, haemodynamic parameters and extubation quality in patients who had adenotonsillectomy surgery using sevoflurane anaesthesia.

2 | METHODS

The study was approved by the local ethics committee and written informed consent was obtained from the parents or guardians of all paediatric patients. The study was also registered in the Australian New Zealand Clinical Trials Registry (registration number: ACTRN12619001268134) and was performed in accordance with the Declaration of Helsinki.

Sixty paediatric patients who had undergone adenotonsillectomies were included in this randomized double-blind clinical study. The patients were between 2 and 9 years old and had American Society of Anesthesiologists (ASA) grades of I or II. A computer-generated scheme was used to randomize the patients into either the dexmedetomidine or tramadol groups. Patients with a history of any chronic disease, an ASA grade of III or higher, blood pressure of <100/50 mm Hg, heart rate of <60 bpm or a known allergy to study

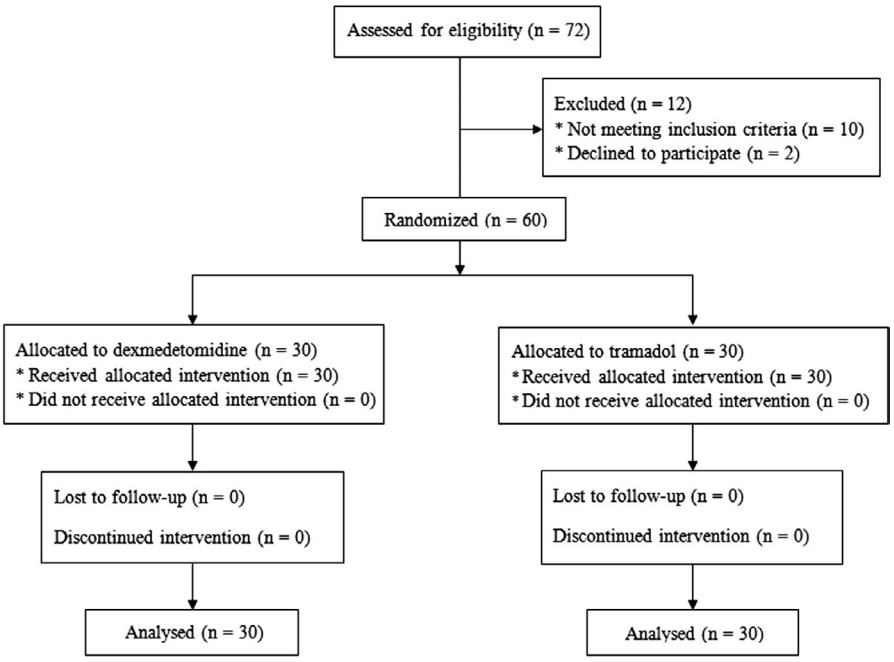

FIGURE 1 Flow diagram of the study

medications were excluded. The flow diagram of the study is shown in Figure 1.

Patients were taken to the pre-operative preparation room with their parents/guardians about 30 minutes prior to surgery. Midazolam was administered orally at a dose of 0.4 mg/kg to all patients in the pre-operative preparation room. The patients were subsequently monitored and taken into the operation room.

The mean arterial pressure (MAP) and heart rate (HR) of all patients were monitored and recorded. Induction of anaesthesia was performed using 8% sevoflurane in 50% nitrous oxide and 50% oxygen. After the induction of anaesthesia, the concentration of sevoflurane was gradually decreased. An intravenous (iv) catheter was then inserted, and an infusion of isotonic sodium chloride (6 mg/kg/h) was started. To facilitate endotracheal intubation, fentanyl and rocuronium were administered iv at a dose of 1 μg/kg and 0.05 mg/kg, respectively. A spiral cuffed tube was used for endotracheal intubation. Anaesthesia was maintained with 2% sevoflurane in 50% nitrous oxide and 50% oxygen. No additional anaesthetic agents were used.

Patients randomized into the dexmedetomidine group (group D, n = 30) and the tramadol group (group T, n = 30) received 1 μg/kg dexmedetomidine or 1.5 mg/kg tramadol, respectively. Both drugs were prepared by a blinded anaesthesia technician, and the iv infusion was administered for 10 minutes prior to the end of surgery. The MAP and HR were recorded at defined time points: T0 (basal, before induction), T1 (20 minutes after induction), T2 (immediately before study drug D or T infusion), T3 (5 minutes after initiation of the study drug infusion), T4 (10 minutes after initiation of the study drug infusion), T5 (first minute post-extubation), T6 (15 minutes after the start of the post-operative period) and T7 (30th minute after the start of the post-operative period).

At the end of the surgery, the volatile anaesthetic was discontinued and oxygen was administered at 6 L/min. Atropine at a dose of 0.015 mg/kg and neostigmine 0.03 mg/kg were used for decurarization. The trachea was extubated upon achieving adequate respiration and was evaluated by observing eye opening and/or response to commands. Extubation time was defined as the time from discontinuation of the inhalation agent to removal of the endotracheal tube. Eye-opening time was defined as the time from discontinuation of the inhalation agent to eye opening with verbal stimulation. Not breathing (>20 seconds), cough-bucking (frequency ≥4), desaturation (O_2 saturation <95%) and the presence of nausea or vomiting after the extubation period were recorded for all patients.

Patients were then transferred to the post-anaesthesia care unit (PACU) and monitored for 30 minutes to evaluate the early post-operative period. The MAP and HR were continually monitored in the PACU. The Riker Sedation-Agitation Scale (SAS) was used to determine the level of anxiety in patients, and the pain point system scale (PPSS) was used to measure the level of pain in patients.[14,15] The Riker SAS and PPSS were the primary endpoints of the study, and extubation time, extubation quality, MAP and HR were secondary endpoints.

2.1 | Statistical analysis

According to the power analysis with an alpha error of 0.05 and a power of 80%, it was calculated that 30 patients in each group would suffice. Statistical analysis was performed using the NCSS (Number Cruncher Statistical System) 2007 Statistical Software. The Kolmogorov-Smirnov test was used to determine the normality of the continuous variables. Continuous variables were expressed as mean ± standard deviation and compared using Student's *t* test. Categorical variables were expressed as percentages and compared using the chi-square test. The analysis of variance (ANOVA) test was used to compare repeated measurements. *Post hoc* comparison in each group was performed using the Tukey HSD and/or LSD, if suitable. A *P* value of <.05 was considered statistically significant.

3 | RESULTS

Sixty patients were included in this study: 30 patients in group D (dexmedetomidine) and 30 patients in group T (tramadol). The baseline characteristics of the study groups are listed in Table 1. There was no difference between the two groups in terms of age, gender, weight, sex or duration of anaesthesia.

The HR and MAP of patients at each time point are shown in Figure 2A-B. After administration of the study drugs, the HR was significantly lower at T3, T4, T5, T6 and T7 compared with T0 in patients who received dexmedetomidine. However, the HR did not significantly change in patients who received tramadol. In addition, the HR was significantly lower in patients receiving dexmedetomidine compared with tramadol at T3, T4, T5, T6 and T7 (Figure 2A). The MAP was significantly lower at T3 and T4 compared with T0 in both. However, there was no significant difference in the MAP

TABLE 1 Comparison of baseline characteristics of patients in each study group

	Dexmedetomidine group (n = 30)	Tramadol group (n = 30)	*P* value
Age, years	6.17 ± 2.07	5.4 ± 2.19	.169
Male gender (%)	14 (46.7)	14 (46.7)	.999
Weight (kg)	22.77 ± 5.94	19.6 ± 7.24	.069
Duration of anaesthesia (min.)	48.1 ± 10	44.7 ± 7.51	.142

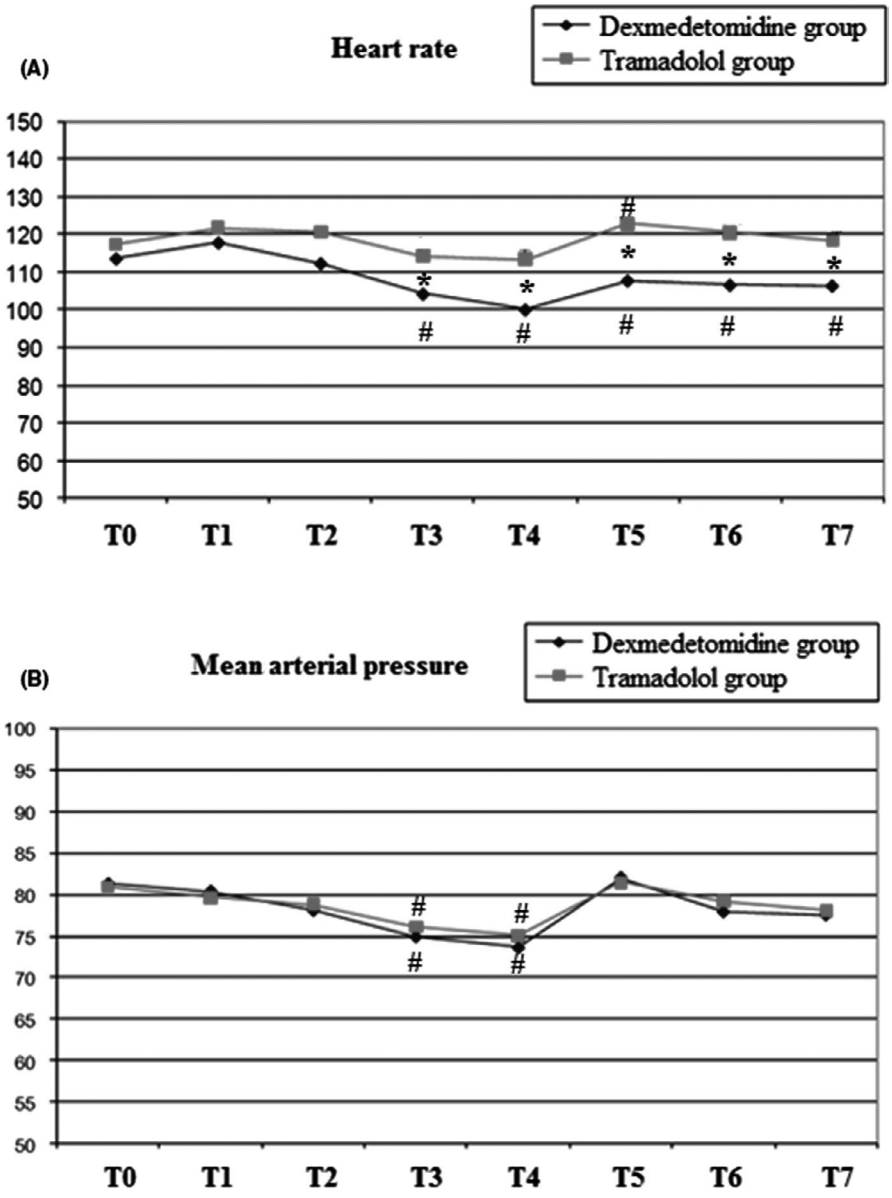

FIGURE 2 A-B: Comparison of heart rate (A) and mean arterial pressure (B) in patients treated with dexmedetomidine or tramadol. T0, before induction (basal); T1, 20 min after induction during the procedure; T2, immediately before study drug infusion (dexmedetomidine or Tramadol); T3, 5th min during study drug infusion; T4, 10th min during study drug infusion; T5, 1st min post-extubation; T6, 15th min during post-operative period; T7, 30th min during post-operative period. *P < .05: difference between the two groups at the same time points. #P < .05: comparison of time points with T0 within the same group

TABLE 2 Comparison of extubation time and adverse events after extubation in the post-operative period

	Dexmedetomidine group (n = 30)	Tramadol group (n = 30)	*P* value
Extubation time (min.)	5.33 ± 3.23	3.47 ± 0.86	.003
Eye-opening time (min.)	11.2 ± 4.72	8.47 ± 1.57	.004
Not breathing, cough-bucking or desaturation after extubation	1 (3.3)	6 (20)	.044
Nausea or vomiting after extubation	1 (3.3)	6 (20)	.044

between the two groups when comparing values at the same time points (Figure 2B).

Not breathing, cough-bucking and desaturation after extubation were significantly lower in patients who received dexmedetomidine compared with patients who received tramadol (3.3% vs 20%, P = .044). Similarly, nausea and vomiting after extubation were significantly lower in patients who received dexmedetomidine compared with tramadol (3.3% vs 20%, P = .044). However, the time to extubation (5.33 ± 3.23 vs 3.47 ± 0.86 minutes, P = .003) and eye-opening time (11.2 ± 4.72 vs 8.47 ± 1.57 minutes, P = .004) were significantly longer in patients who received dexmedetomidine compared with tramadol (Table 2).

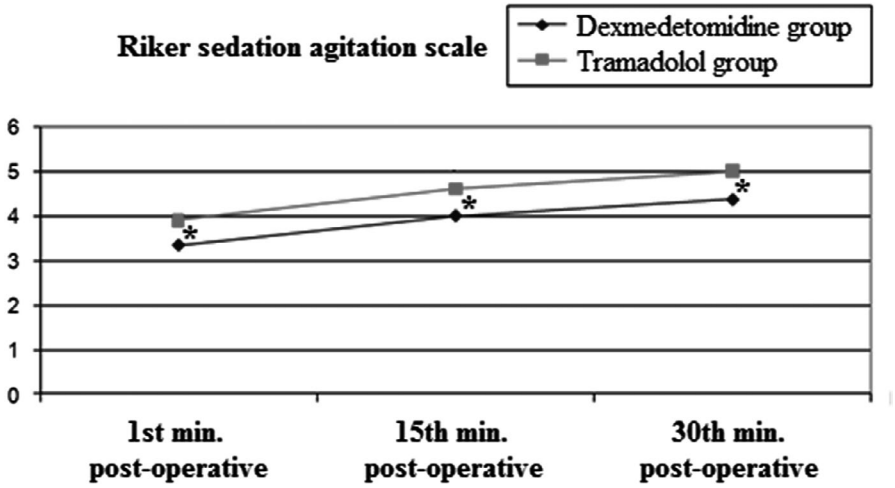

FIGURE 3 Comparison of Riker Sedation-Agitation Scale results in patients treated with dexmedetomidine or tramadol

The post-operative Riker SAS and PPSS results are shown in Figure 3 and Figure 4, respectively. The post-operative Riker SAS was significantly lower for patients who received dexmedetomidine than for patients who received tramadol at the post-operative time points 1, 15 and 30 minutes. Similarly, the PPSS was significantly lower in the dexmedetomidine group than in the tramadol group at the post-operative time points 1, 15 and 30 minutes. Serious adverse events such as respiratory depression, haemodynamic instability, hypotension and bradycardia were not observed in any patients.

4 | DISCUSSION

In this study, the effects of dexmedetomidine or tramadol on post-operative pain and agitation, extubation quality and haemodynamic parameters were compared in paediatric patients who underwent adenotonsillectomy surgery with sevoflurane aesthesia. The main findings of our study were as follows: (a) the use of dexmedetomidine was associated with lower levels of post-operative pain and agitation compared with tramadol; (b) although extubation and eye-opening times were significantly longer, it was observed that the extubation quality was better with dexmedetomidine; and (c) the use of dexmedetomidine was associated with a greater decline in heart rate compared with tramadol.

Adenotonsillectomy is one of the most commonly performed surgical procedures in childhood. However, the post-operative period is exhausting for patients, and many suffer from post-operative pain and agitation.[1,2] Pain is more commonly felt during recovery after anaesthesia and may lead to reduced oral intake, dehydration and agitation. Agitation may also cause self-injury, with results such as haemorrhaging at the surgical site.[4-6] Since post-operative pain and agitation may be associated with serious complications and longer hospitalization times, it is important to control pain effectively during adenotonsillectomy surgeries. However, there is limited information on which agent should be used during surgery. The optimal drug should provide effective pain control, have minimal adverse effects and facilitate rapid recovery.

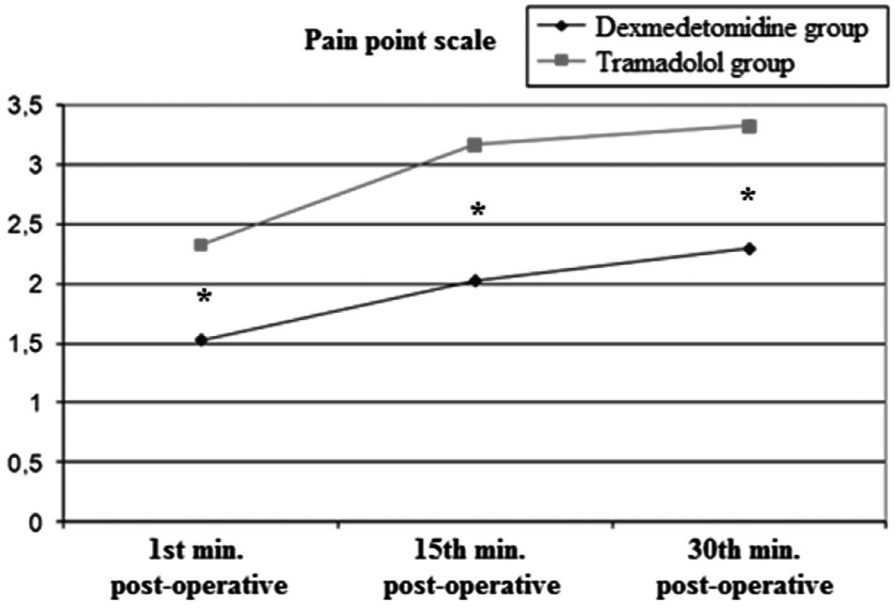

FIGURE 4 Comparison of pain point scale results in patients treated with dexmedetomidine or tramadol

Opioids and alpha-2 receptor agonists can be administered to decrease post-operative pain and agitation. Tramadol is one opioid that is commonly used to treat pain. However, tramadol causes adverse effects such as nausea, vomiting and respiratory depression.[12] Dexmedetomidine is another alpha-2 receptor agonist that has sympatholytic, sedative and analgesic effects.[7] Previous studies have shown that dexmedetomidine could be used as a sedative in the paediatric intensive care unit and as an adjunct to volatile anaesthetics.[2,16] It has also been demonstrated that dexmedetomidine decreases post-operative pain and agitation.[17] For these reasons, dexmedetomidine may be effectively used to treat post-operative pain and agitation in children undergoing adenotonsillectomy surgery using sevoflurane.

In a recent meta-analysis, the effects of perioperative dexmedetomidine used an adjuvant during an adenotonsillectomy was compared with the use of opioid or placebo in paediatric patients who underwent adenotonsillectomy surgery.[2] It was found that dexmedetomidine significantly lowered post-operative pain and the need for analgesic drugs compared with the control group. In addition, the frequency of oxygen desaturation was significantly lower. A subgroup analysis showed that dexmedetomidine decreased the severity and frequency of agitation more effectively than other opioids. Only one study in this meta-analysis compared the effects of dexmedetomidine and tramadol; it found that both tramadol and dexmedetomidine were effective for controlling pain and the emergence of agitation.[18] Similarly, we also showed that post-operative pain and agitation were significantly lower in patients who received dexmedetomidine compared with tramadol. Based on these results, we conclude that dexmedetomidine provides more effective pain and agitation control than tramadol in paediatric patients who undergo adenotonsillectomy surgery using sevoflurane. Although these studies compared the effects of dexmedetomidine and tramadol on post-operative pain and agitation, the effects of these two drugs on extubation quality were not evaluated.

Nausea and vomiting are common complications after adenotonsillectomy operations because blood is frequently swallowed, resulting in irritation in the oropharynx.[19] We found that the frequency of nausea and vomiting was significantly lower in patients treated with dexmedetomidine. Moreover, not breathing, cough-bucking and desaturation after extubation were significantly lower in patients treated with dexmedetomidine. However, the time to extubation and eye-opening time were significantly longer after dexmedetomidine treatment compared with tramadol. These results suggest that although dexmedetomidine is associated with longer extubation time, it provides a better extubation quality than tramadol.

Hypotension and bradycardia are the most common haemodynamic adverse effects associated with the sympatholytic effects of dexmedetomidine.[20,21] We found that although the MAP was not significantly different between patients in the dexmedetomidine and tramadol groups, HR was significantly lower in the dexmedetomidine group. These results suggest that bradycardia may be more common with the use of dexmedetomidine. Nevertheless, we did not detect hypotension or bradycardia in any group during the follow-up period. This may be due to using relatively low doses of dexmedetomidine.

The main limitation of our study was the small sample size. In addition, we used only the Riker SAS to score agitation in this study. Many other scales could be used; using multiple scales and comparing the results might provide additional insights. Further studies with a larger sample size are required for a clearer understanding of the effects of dexmedetomidine and tramadol on post-operative recovery in paediatric patients.

5 | WHAT IS NEW AND CONCLUSION

We demonstrated that dexmedetomidine was more effective than tramadol for controlling post-operative pain and agitation in paediatric patients undergoing adenotonsillectomy surgery using sevoflurane. In addition, although it was associated with longer extubation time, dexmedetomidine provided a better extubation quality than tramadol. However, it should be taken into consideration that patients who receive dexmedetomidine should be more closely monitored for bradycardia.

CONFLICT OF INTEREST

None to declare.

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