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Pain Relief for Children after Adenotonsillectomy

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Effective pain relief following adenotonsillectomy in children remains a challenge. This study evaluated the effects of intramuscular 0.5 mg/kg ketamine, 1 mg/kg tramadol or 1 mg/kg meperidine on post-operative pain and recovery in 45 children aged 1 – 7 years undergoing adenotonsillectomy. Anaesthesia was induced with thiopental or sevoflurane (with succinylcholine for intubation) and was maintained with sevoflurane in oxygen and nitrous oxide. Post-operative pain was scored blind using a modified Toddler–Preschooler Post-Operative Pain Scale 30, 60, 120 and 240 min after tracheal extubation. Post-operative agitation scores were also recorded. Mean post-operative pain score was significantly higher in the tramadol-treated group compared with the meperidine-treated group 120 min after extubation. At all other time-points after extubation, mean post-operative pain scores were similar for the three treatment groups. Ketamine was associated with a significantly higher mean agitation score compared with tramadol and meperidine. We conclude that the effects of ketamine, meperidine and tramadol on post-operative pain following adenotonsillectomy in children were similar.

KEY WORDS: Meperidine; Ketamine; Tramadol; Analgesics; Adenotonsillectomy; Children; Post-operative pain; Agitation

Introduction

Post-operative pain is common after tonsillectomy and adenoidectomy. Unfortunately, post-operative pain is often intense, so most children require some opioid analgesia even if paracetamol is given pre-operatively. However, opioids may cause respiratory depression, sedation, and nausea and vomiting. Post-operative pain relief in children remains an unresolved problem.[1]

Administration of opioids, non-steroidal anti-inflammatory drugs (NSAIDs) or local anaesthetics together with pre-medication before induction of general anaesthesia is common practice.[1] The analgesic effect of NSAIDs is often insufficient and these agents may cause increased pre-operative and post-operative bleeding, so they are not usually recommended for post-operative pain relief in children.[2,3]

Ketamine is a non-competitive antagonist of the *N*-methyl-D-aspartate (NMDA) receptor that has analgesic properties at sub-anaesthetic doses,[4] but there are few studies comparing ketamine with other analgesics for post-operative pain relief in children.

Tramadol has a low affinity for opioid receptors, but it also exerts its effects by direct

modulation of central monoaminergic pathways. It is a weak opioid analgesic with a potency that is similar to that of meperidine. Tramadol is a well-tolerated and effective post-operative analgesic in children older than 1 year and is associated with adverse effects that are similar to those of other opioids.[5] The recommended dose of tramadol for children is 1 – 2 mg/kg, three or four times daily. Whether higher doses of tramadol improve analgesia without increasing adverse events in the paediatric population warrants further investigation.[6]

Meperidine is a synthetic narcotic analgesic that undergoes hepatic metabolism. The onset of action of meperidine occurs at 15 – 30 min, with a peak effect at 45 – 60 min, and its duration of action is up to 4 h.[7,8] Side-effects associated with meperidine use include respiratory and central nervous system depression, seizures, nausea and vomiting.

The purpose of this study was to evaluate the effects of ketamine, tramadol and meperidine on post-operative pain and recovery in children undergoing adenotonsillectomy.

Patients and methods

PATIENTS

Children scheduled for tonsillectomy with or without adenoidectomy were included in the study. Patients were excluded if they had a known allergy to the study drugs, asthma, kidney or liver dysfunction, or haemorrhagic diathesis. All children were American Society of Anesthesiologist (ASA)[9] Physical Status I – II and were aged 1 – 7 years. The study was approved by the local ethics committee of Akdeniz University Faculty of Medicine, and all parents provided informed consent for their child's participation in the study.

ANAESTHESIA AND SURGERY

All children were pre-medicated with 0.3 mg/kg midazolam intranasally for 20 min before induction of general anaesthesia. After application of routine non-invasive monitoring devices (blood pressure, electrocardiogram, pulse oximeter), a standardized general anaesthetic agent was administered. Anaesthesia was induced with 5 – 7 mg/kg thiopental intravenously, or if venous access could not be performed, 8% sevoflurane and 50% nitrous oxide in oxygen was administered by inhalation. Tracheal intubation was facilitated using 1.5 mg/kg succinylcholine. After induction of anaesthesia and before tracheal intubation, children were randomly allocated to receive 0.5 mg/kg ketamine, 1 mg/kg meperidine or 1 mg/kg tramadol, administered as an intramuscular injection into the anterolateral aspect of the thigh.

Anaesthesia was maintained with 2% sevoflurane and 50% nitrous oxide in oxygen. Heart rate was recorded at regular intervals: before and after induction of anaesthesia; after tracheal intubation; 10, 20 and 30 min into the operation; and at the end of surgery. Administration of all inhaled anaesthetic agents was terminated at the end of surgery. Each patient's trachea was extubated when they had a cough and gag reflex, grimace and purposeful movements. Signs and symptoms of airway irritability (laryngospasm, coughing) during emergence from anaesthesia were recorded by an investigator who was not blinded to the drugs. The time to opening the eyes upon command was noted. Post-operative vomiting and agitation during emergence from anaesthesia were recorded. The tonsils and adenoids were removed using dissection and diathermy.

ASSESSMENT OF POST-OPERATIVE PAIN

The anaesthetists in the recovery room, the ward nurses and the score observers were blinded to the identity of the study drugs. Post-operative pain was assessed in the

recovery room 30, 60, 120 and 240 min after tracheal extubation by a blinded observer using a modified Toddler–Preschooler Post-operative Pain Scale (TPPPS),[10] with a maximum score of 10 (Table 1). Post-operative agitation was assessed using a three-point scale: 1 = calm; 2 = agitated but consolable; and 3 = severely agitated and inconsolable. Emergence agitation was considered to be grade 3 agitation.

STATISTICAL ANALYSIS

Statistical analysis was performed using the Kruskal–Wallis test, Mann–Whitney *U*-test, χ^2 test and independent samples *t*-test. Power analysis was performed with NCSS 2000 and PASS 2000 software (NCSS Statistical Software, Kaysville, Utah, USA) and the power of the study was 85%. *P*-values < 0.05 were considered to be statistically significant.

Results

A total of 45 children were randomized to the three study groups (n = 15 per group). There was no significant difference between the groups with respect to age, gender, body weight and duration of surgery (Table 2).

The mean modified TPPPS score was significantly higher in the tramadol-treated group compared with the meperidine-treated group only at 120 min after extubation ($P < 0.05$) (Table 3). At all other time-points

TABLE 1:
The modified Toddler–Preschooler Post-operative Pain Scale (TPPPS)[10] used to assess pain in paediatric patients following tonsillectomy with or without adenoidectomy

	Modified TPPPS[a]		
Observation	**Score 0 points**	**Score 1 point**	**Score 2 points**
Verbal complaint/cry	None	Once only	> Once
Groan/moan/grunt	None	Once only	> Once
Facial expression	Neutral	One grimace	Grimace > once
Restless motor behaviour	None	One episode only	> One episode
Rub/touch painful area	None	Once only	> Once

[a]Score is awarded per observation with a maximum cumulative score of 10.

TABLE 2:
Demographic data and duration of surgery in paediatric patients receiving intramuscular injections of 0.5 mg/kg ketamine, 1 mg/kg meperidine or 1 mg/kg tramadol for pain relief after tonsillectomy with or without adenoidectomy

	Ketamine group (n = 15)	**Meperidine group (n = 15)**	**Tramadol group (n = 15)**
Age (years)	4.26 ± 1.57	3.93 ± 1.66	4.07 ± 1.54
Body weight (kg)	13.53 ± 2.29	12.93 ± 1.94	13.21 ± 2.00
Gender (male/female)	7/8	6/9	5/10
Duration of surgery (min)	39.33 ± 5.93	37.00 ± 6.21	38.33 ± 8.38

Values are mean ± SD or number.

TABLE 3:
Mean post-operative pain and agitation scores, and time to opening eyes on command in paediatric patients receiving intramuscular injections of 0.5 mg/kg ketamine, 1 mg/kg meperidine or 1 mg/kg tramadol for post-operative pain relief after tonsillectomy with or without adenoidectomy

	Ketamine group (n = 15)	Meperidine group (n = 15)	Tramadol group (n = 15)
Modified TPPPS score after extubation			
30 min	2.93 ± 0.70	2.66 ± 0.75	3.07 ± 0.73
60 min	1.80 ± 0.67	1.60 ± 0.82	2.07 ± 0.73
120 min	1.73 ± 0.70	1.46 ± 0.83	2.14 ± 0.36[a]
240 min	1.13 ± 0.83	0.93 ± 0.70	1.28 ± 0.91
Agitation score	2.00 ± 0.65[b]	1.26 ± 0.45	1.21 ± 0.42
Time to opening eyes upon command (min)	9.8 ± 3.27	7.1 ± 2.66	7.4 ± 2.61

Values are mean ± SD.
TPPPS, Toddler–Preschooler Post-operative Pain Scale.
[a]$P < 0.05$ tramadol-treated group versus meperidine-treated group at the same time-point.
[b]$P < 0.05$ ketamine-treated group versus the meperidine- and tramadol-treated groups.

after extubation, the mean modified TPPPS scores were similar for the three treatment groups.

There were no significant differences between the groups with respect to time to opening eyes upon command (Table 3).

The mean post-operative agitation score was significantly higher in the ketamine-treated group compared with the meperidine- and tramadol-treated groups ($P < 0.05$) (Table 3).

Vomiting occurred in two (13.3%) children treated with ketamine, three (20.0%) children treated with meperidine and three (20.0%) children treated with tramadol. There was no significant difference in the incidence of vomiting between the three treatment groups.

Heart rates during anaesthesia of children in the ketamine-treated group were significantly higher than the rates for children in the meperidine- and tramadol-treated groups (Fig. 1) ($P < 0.05$).

The incidence of post-operative laryngospasm was similar in the three treatment groups. Laryngospasm occurred in six (40%) children treated with ketamine, two (13.3%) children treated with meperidine and five (33.3%) children treated with tramadol.

Discussion

The treatment of post-operative pain following day-case paediatric surgery provides a great challenge to medical staff. Children should be pain-free and alert on discharge from hospital, but more then 80% of children require pain medication after day-case surgical procedures.[11]

Few studies have been done in paediatric populations, although ketamine, meperidine and tramadol have been shown to be useful for post-operative pain control when administered at different doses and by different routes.[5,12–17]

The recommended dose of tramadol for children is 1 – 2 mg/kg; we used a dose of 1 mg/kg in this study. The relative lack of

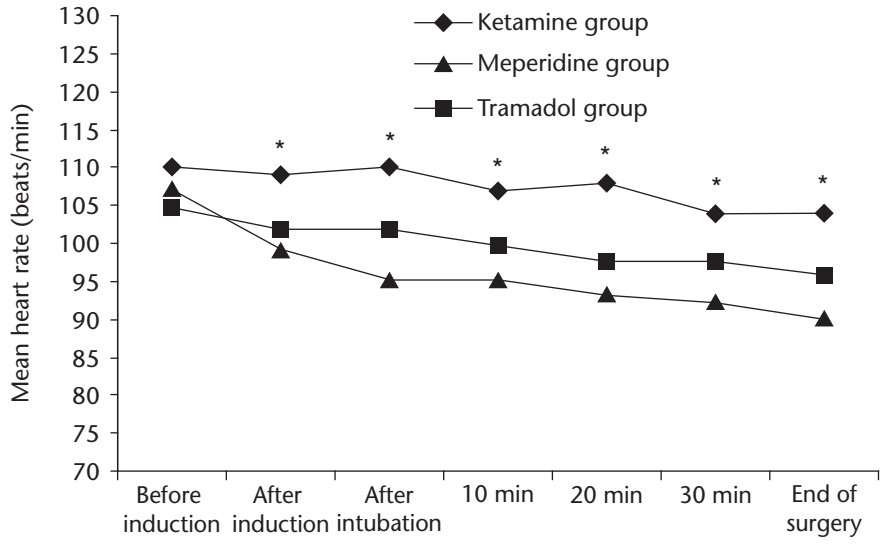


FIGURE 1: Mean changes in heart rate (before and after induction of anaesthesia; after tracheal intubation; 10, 20 and 30 min into the operation; and at the end of surgery) in paediatric patients receiving intramuscular injections of 0.5 mg/kg ketamine, 1 mg/kg meperidine or 1 mg/kg tramadol for post-operative pain relief following tonsillectomy with or without adenoidectomy. *$P < 0.05$ versus meperidine- and tramadol-treated groups

sedative effects and respiratory depression associated with tramadol has resulted in its use as an alternative to traditional opioids for post-operative pain control in children.[12] Although tramadol is an alternative opioid for post-operative pain control, we did not find any significant differences in the post-operative pain scores among the three treatment groups at any time-point except 120 min after extubation. The 120-min pain score was significantly higher in the tramadol-treated group compared with the meperidine-treated group ($P < 0.05$).

Studies that compare ketamine with other analgesics in children are limited. Murray *et al.*[18] showed that 0.5 mg/kg intravenous ketamine provided better analgesia than placebo after tonsillectomy in children. This present study found that ketamine treatment was associated with post-operative pain scores similar to those for tramadol and meperidine. The study demonstrated a significant increase in heart rate in the ketamine-treated group during anaesthesia compared with the meperidine- and tramadol-treated groups ($P < 0.05$).

The post-operative agitation score was also significantly higher in the ketamine-treated group compared with the meperidine- and tramadol-treated groups ($P < 0.05$). The aetiology of emergence agitation is unknown. Murray *et al.*[19] demonstrated that oxycodone pre-medication reduced the frequency of agitation in children who received halothane, but not in children who received sevoflurane for general anaesthesia. Kararmaz *et al.*[20] demonstrated that administration of oral ketamine significantly reduced the incidence of

emergence agitation after desflurane anaesthesia in children undergoing adenotonsillectomy. The agitation observed in the children treated with ketamine resolved spontaneously without any medication.

No adverse effects, such as sedation and respiratory depression, were observed and the incidence of vomiting was similar among the three groups, but this effect might have been due to the residual effect of the general anaesthesia.

We conclude that ketamine, meperidine and tramadol had very similar effects on post-operative pain after adenotonsillectomy in children. They provided adequate post-operative analgesia in paediatric patients undergoing day-case adenotonsillectomy. During the emergence from anaesthesia, the higher agitation scores may be a limiting factor in the use of ketamine after adenotonsillectomy in children.

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Conflicts of interest

No conflicts of interest were declared in relation to this article.

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