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ORIGINAL ARTICLE

Analgesic efficacy of topical tramadol in the control of postoperative pain in children after tonsillectomy

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Abstract
Purpose Pain control after tonsillectomy is still a controversial issue. Topical approaches have the advantage of pain control with good patient acceptability. Therefore, this study was conducted to evaluate the effects of topical tramadol on postoperative pain and morbidity in children undergoing tonsillectomy.
Methods A prospective, randomized, double-blind, controlled clinical study was designed. Forty children aged between 4 and 15 years, ASA I–II, scheduled for elective tonsillectomy and/or adenoidectomy were randomized into two groups. For patients in Group T ($n = 20$) swabs soaked with 2 mg/kg tramadol diluted in 10 ml saline were applied to both of their tonsillar fossa for 5 min; in the control group ($n = 20$) swabs soaked with 10 ml saline were applied. Postoperative pain scores, bleeding, nausea, vomiting, abdominal discomfort, constipation, pain in the throat, painful swallowing, fever, otalgia, trismus, and halitosis were recorded at the first, fifth, thirteenth, seventeenth, twenty-first, and twenty-fourth postoperative hours and the week after tonsillectomy.
Results Pain scores were found to be significantly lower at the 21st hour and on postoperative day seven in the tramadol group compared with the control group ($p < 0.05$). Mean daily pain scores ranged from Day 1: 0.34 (±0.21) to Day 7: 0.11 (±0.08) in the tramadol group and Day 1: 0.53 (±0.14) to Day 7: 0.42 (±0.15) in the control group. There were no significant differences in morbidity between the groups ($p > 0.05$).
Conclusion Topical 5% tramadol with its local anesthetic effect seems to be an easy, safe, and comfortable approach for pain management in children undergoing tonsillectomy.

Keywords Pain · Tonsillectomy · Topically · Tramadol

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Introduction

Tonsillectomy is one of the most common day-case surgical procedures carried out on children. Significant pain associated with tonsillectomy is reported in 20–50% of children undergoing tonsillectomy [1]. Despite the use of different surgical techniques, the problem of effective post-tonsillectomy pain relief remains a clinical challenge [2]. According to a study including 129 children aged between 5 and 16 years, substantial pain that lasted more than 7 days after tonsillectomy was recorded. The children reported pain as moderately intense for the first 3 days followed by a gradual decline over the next 4 days [3]. This pain may cause poor oral intake, long hospital stay, and delay in return to normal activities. In general it has been controlled with morphine, resulting in a high incidence of postoperative nausea and vomiting (PONV) compared with other forms of analgesia [4].

Umuroglu compared the analgesic effects of intravenously administered morphine, ketamine, and tramadol for adenotonsillectomy in children. They found the analgesic effect of morphine 0.1 mg/kg intravenously administered during induction of anesthesia superior to tramadol and ketamine [5]. Undesired side effects, for example respiratory depression, and sedation, caused by morphine may

also be hazardous after tonsillectomy. All these side effects force clinicians to develop alternative analgesic strategies.

Topical approaches have the advantage of local pain control with minimal systemic side-effects and good patient acceptability. Local anesthetics, antihistamines, anti-inflammatory agents, and opioids are given in solution form by rinsing throughout the oral cavity for oropharyngeal pain control. For this reason we suggested a topical route for pain management.

Tramadol is formulated as a racemic mixture with each enantiomer having different opioid receptor-binding properties, monoaminergic reuptake inhibition, and metabolic pathways. Tramadol has methyl group substitution on the phenolic moiety, which explains its weak affinity for opioid receptors. Tramadol was initially reported to lack selectivity for μ, κ, and δ-receptors, but it has been demonstrated to be selective for the μ-receptor. Furthermore the M1 metabolite of tramadol, which is produced by *o*-demethylation, has greater affinity for opioid receptors than the parent drug [6]. In addition, tramadol has been proved to exert a local anesthetic effect on peripheral nerves in both clinical and laboratory studies. The mechanism of action of tramadol is similar to that of hydrophobic local anesthetics [7].

The purpose of this study was to assess the effects of topical tramadol on postoperative pain relief in children after tonsillectomy.

Materials and methods

Following approval of the research by the ethics committee of the hospital, and after informed written parental consent had been obtained, 40 children aged between 4 and 15 years, ASA I–II, scheduled for elective tonsillectomy and/or adenoidectomy were randomized by the sealed-envelope technique into two groups with 20 patients in each. All operations were performed by the same surgeon, who was blind to the study drug, using a standardized snare dissection technique. The patients were suffering from recurrent tonsillitis, chronic tonsillitis, OSAS (obstructive sleep apnea syndrome), tonsillar hypertrophy, or dysphagia. Exclusion criteria included a known allergy, sensitivity, or contra-indication to opioids or local anesthetic, renal or liver impairment, acute pharyngeal infection, a history of asthma, or clotting disorder.

All patients were fasted and premedicated. Patients aged between 4 and 6 years were premedicated with midazolam 0.5 mg/kg by the rectal route and patients aged over 6 years were premedicated with oral midazolam 0.5 mg/kg in 10 ml juice. Patients were operated under general anesthesia by use of a standardized procedure. Routine monitoring (ECG, noninvasive blood pressure, oxygen saturation, end-tidal CO_2, and temperature) was used. After induction with propofol 2 mg/kg and atracurium 0.5 mg/kg, anesthesia was maintained with propofol 2 mg/kg/h and remifentanil 0.1 μg/kg/min intravenously.

After tonsillectomy, swabs soaked with 2 mg/kg tramadol diluted in 10 ml saline were applied for 5 min to both tonsillar fossa of the patients in Group T ($n = 20$); for the patients in the control group ($n = 20$) the swabs were soaked with 10 ml saline. Hemostasis, if required, was by compression and silk ligature.

Paracetamol (20 mg/kg) and amoxicillin (45 mg/kg) oral pediatric suspensions were given every 6 h to all patients as a routine clinical procedure.

Patients were evaluated using an eight-item questionnaire and McGrath's visual scale (Fig. 1). McGrath's face scale has nine happy–sad faces which define the level of pain ranging from no pain to a lot of pain [8]. All tonsillectomy complaints (for example bleeding, nausea, vomiting, abdominal discomfort, constipation, pain in the throat, painful swallowing, fever, otalgia, trismus, and halitosis) and pain scores were recorded on the first day (at the first, fifth, thirteenth, seventeenth, twenty-first, and twenty-fourth postoperative hours) and during the week after tonsillectomy by their parents.

A sample size of 17 per group was required for analysis of the pain scores with a power of 80% at a 5% significance level. The target pain score was 0.15 in both the tramadol and control groups when calculating the power. Data from forty patients were analyzed with SPSS 10.0 software (SPSS, Chicago, IL, USA) for Windows. Student *t* and chi-squared tests were used for statistical analysis of the data. Analysis of variance was used to assess changes in postoperative pain as reported by the children from day 1 to day 7. Data were expressed as mean ± standard deviation (SD). A p value of <0.05 was accepted as significant.

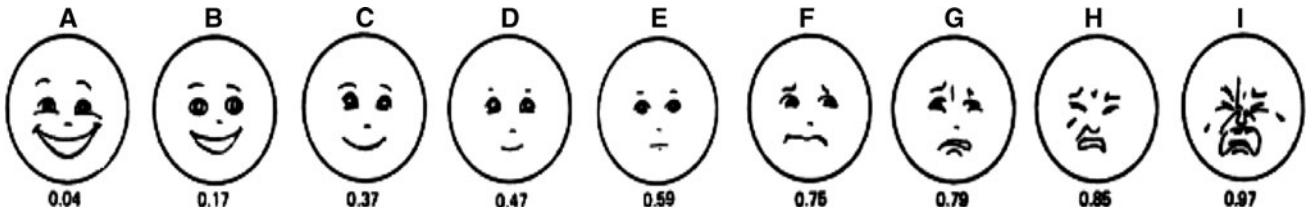

Fig. 1 McGrath's face scale (happy–sad nine-face scale)

Results

There were no statistically significant differences between age, gender, and ASA physical status for the groups ($p > 0.05$) (Table 1).

Pain scores decreased with time in both groups ($p < 0.05$). They were found to be significantly lower after 21 h in the tramadol group compared with the control group ($p < 0.05$). The pain scores were significantly lower in the tramadol group than the control group at postoperative day 7 follow-up ($p < 0.05$). Mean daily pain scores ranged from Day 1: 0.34 (±0.21) to Day 7: 0.11 (±0.08) in the tramadol group and Day 1: 0.53 (±0.14) to Day 7: 0.42 (±0.15) in the control group (Table 2).

Table 1 Patient characteristics (mean ± SD)

	Group C, $n = 20$	Group T, $n = 20$	p value
Age (year)	7.7 ± 3.7	7.7 ± 2.6	>0.05
Gender (F/M)	5/15	8/12	>0.05
ASA (I/II)	20/0	16/4	>0.05

Table 2 Mean pain scores (±SD) for the tramadol and control groups

Pain score at	Group C	Group T	p value
1 h	0.85 ± 0.11	0.80 ± 0.25	>0.05
5 h	0.75 ± 0.12	0.72 ± 0.11	>0.05
13 h	0.65 ± 0.13	0.62 ± 0.14	>0.05
17 h	0.59 ± 0.12	0.51 ± 0.12	>0.05
21 h	0.53 ± 0.14	0.34 ± 0.21	**<0.05**
Second day	0.51 ± 0.11	0.38 ± 0.16	**<0.05**
Third day	0.52 ± 0.17	0.34 ± 0.17	**<0.05**
Fourth day	0.46 ± 0.13	0.28 ± 0.15	**<0.05**
Fifth day	0.44 ± 0.12	0.24 ± 0.13	**<0.05**
Sixth day	0.42 ± 0.15	0.15 ± 0.12	**<0.05**
Seventh day	0.42 ± 0.15	0.11 ± 0.08	**<0.05**

There were no significant differences in nausea, vomiting, halitosis, trismus, fever, otalgia, and bleeding scores between the groups ($p > 0.05$) (Table 3).

Discussion

The oropharynx and the tonsillar fossae are innervated locally by the branches of the trigeminal and glossopharyngeal nerves which are highly represented in the somatic cerebral cortex. Topical administration of local anesthetic agents reduces pain by producing pharmacologic blockade of the sensory pathways. Previous studies determined that topical 1% ropivacaine provided superior postoperative analgesia, as reflected by lower recovery room pain scores and opioid requirements [9].

In addition to local anesthetics, opioids and hypnotic agents, for example ketamine, have been found to be useful in pain relief for children. Canbay et al. studied 60 children aged between 3 and 12 years undergoing tonsillectomy. With four groups of 15 they compared placebo with ketamine 20 mg, morphine 20 mg, and a mixture of ketamine plus morphine topically. They reported higher pain scores on arrival in the recovery room in the placebo group. They found morphine and ketamine groups had longer effective analgesia time and reduced analgesic requirement on the first postoperative day than the mixture of morphine plus ketamine and control groups [10].

Several studies have suggested that tramadol infiltration resulted in a longer analgesic time than parenteral tramadol [11, 12]. Our study showed that topical administration of 5% tramadol significantly reduced pain scores 21 h after the operation, and at the next week follow-up compared with the control group. Topical tramadol might not have a significant analgesic effect on acute phase pain immediately after the operation. This delayed analgesic effect might be because of topical administration to the tonsillar fossa and dilution of the tramadol.

Table 3 The postoperative and day 7 follow up morbidity records of the groups

Groups	Postop. C vs. T	Day 1 C vs. T	Day 2 C vs. T	Day 3 C vs. T	Day 4 C vs. T	Day 5 C vs. T	Day 6 C vs. T	Day 7 C vs. T	p value
Nausea	7–5	3–5	0–2	0–1	0–1	0–1	0–1	0–1	>0.05
Vomiting	5–2	5–2	1–2	0–1	0–1	0–0	0–1	0–0	>0.05
Bleeding	0–0	0–0	0–0	0-0	0–0	0–0	0–0	0–0	>0.05
Halitosis	6–7	7–7	6–6	3–3	0–1	0–1	0–0	0–0	>0.05
Fever	7–5	4–5	0–3	0–2	0–1	0–1	0–0	0–0	>0.05
Otalgia	3–3	1–2	0–2	1–1	1–2	0–0	0–0	0–0	>0.05
Trismus	0–0	0–0	0–0	0–0	0–0	0–0	0–0	0–0	>0.05

Atef and Fawaz investigated the local anesthetic effect of tramadol on pediatric patients undergoing tonsillectomy. They randomized 40 patients into two groups, and one group was infiltrated submucosally with 2 mg/kg tramadol in 3 ml saline and the other group with saline. They found that the incidence of immediate pain after recovery from anesthesia was low (20%) in the tramadol group. In contrast with our study they reported that the analgesic effect of infiltrated tramadol 2 mg/kg after tonsillectomy is limited to 4 h [13].

Jou et al. [14] reported that tramadol affects sensory and motor nerve conduction by a similar mechanism to that of lidocaine, which acts on the voltage-dependent sodium channel leading to axonal blockage. Mert et al. [7] proposed that tramadol might have a mechanism different from that of lidocaine for producing conduction blocks; the presence of a large Ca^{2+} concentration increases tramadol's activity whereas it reduces lidocaine's activity. Pang et al. suggested a sensory block to pinprick, touch, and cold at the intradermic injection site of 5% tramadol similar to 1% lidocaine [15]. Altunkaya investigated local anesthetic effects of tramadol with prilocaine in sixty patients undergoing excision of cutaneous lesions. They suggested that tramadol has a local anesthetic effect similar to 2% prilocaine when used intradermally [16]. They showed that 5% tramadol may be a good choice for minor surgery, because of its sufficient local anesthetic and analgesic effects. In another study they investigated the efficacy of tramadol for relieving postoperative pain in minor surgery (lipoma excision and scar revision). Forty patients were allocated to two groups; one group received 2 mg/kg tramadol and the other group received 1 mg/kg lidocaine subcutaneously. They found the time span before taking first analgesic medication was longer for the tramadol group than for the lidocaine group [17].

Several adverse effects of tramadol have been reported, including nausea and vomiting. However, as we observed in this study, the incidence of adverse effects in the tramadol group did not differ significantly from those in the control group. Therefore, tramadol is a useful and safe drug for postoperative analgesia with minimal opioid-type adverse effects, e.g. nausea, drowsiness, vomiting, dry mouth, and constipation [18].

In conclusion topical 5% tramadol with its local anesthetic effect seems to be an easy, safe, and comfortable approach for pain management in children undergoing tonsillectomy.

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