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# Preemptive Analgesia with Paracetamol and Tramadol in Pediatric Adenotonsillectomy

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## Abstract

**Introduction:** Pain is a major problem regarding quality of life in children undergoing adenotonsillectomy. Preemptive analgesia is based on administration of an analgesic before a painful stimulus is generated. In this study we compared preemptive efficacy of paracetamol and tramadol in children undergoing adenotonsillectomy.

**Materials and methods:** The study was done between January-May 2009 in ETN operation room. 50 pediatric patients between the ages of 4-12, ASA I-II, were randomly divided into two groups. All patients were premedicated with 0.5 $mg^{-1}$ $kg^{-1}$ midazolam (PO, 30 minute before induction). Anesthesia induction and maintenance were standardized. At induction, in group P the patients received 15 $mg^{-1}$ $kg^{-1}$ paracetamol (infusion in 10 min), in group T the patients received 1 $mg^{-1}$ $kg^{-1}$ tramadol (with 50 mL saline infusion in 10 min). Systolic and diastolic blood pressure (SBP, DBP), heart rate (HR) were obtained during anesthesia. Postoperatively, Aldrete score (time to reach > 9), FLACC (faces, legs, activity, cry, consolability) scores at $0^{th}$, $15^{th}$, $30^{th}$, $45^{th}$, $60^{th}$, $120^{th}$, $180^{th}$, $240^{th}$ minutes and postoperative analgesic requirements were also recorded.

**Results:** No significant differences between groups over all the recorded times of FLACC score. No postoperative analgesic was needed in groups P and T. No significant differences between groups of the mean arterial pressure, heart rate and side effects.

**Conclusion:** Paracetamol and tramadol were found to be efficient preemptive analgesics in adenotonsillectomy of children for postoperative analgesia.

**Keywords:** Preemptive analgesia; Paracetamol; Tramadol; Pediatric anesthesia

## Introduction

Adenotonsillectomy is very common pediatric day-case procedure that is associated with postoperative pain [1]. Preemptive analgesia is based on administration of an analgesic before a painful stimulus is generated, so as to prevent the subsequent rebound mechanism. Significant complications including airway obstruction, protracted vomiting and bleeding can occur after adenotonsillectomy [2]. So, it is important that the patient is awake and able to protect the airway as soon as possible after the surgery. Opioids, due to their associated somnolence, respiratory depression and nausea may contribute to significant postoperative morbidity. Tramadol is an analgesic with mixed-opioid and non-opioid activities. Tramadol offers similar analgesic potential to morphine, however, it has significantly less respiratory depression effects compared to morphine [3,4].

Enteral paracetamol, when used alone, is not very effective for postoperative analgesia because of delayed absorption and sub-therapeutic plasma concentrations [5]. Intravenous formulation of paracetamol has been introduced, and its safety and pharmacokinetic properties have been established for children [6]. This randomized, single- blind, retrospective study was therefore undertaken to compare the postoperative analgesic effects of preemptive administration of intravenous paracetamol as a stand-alone therapy, with those of preemptive intravenous tramadol in pediatric patients undergoing adenotonsillectomy.

## Materials and Methods

After informed consent from a parent for guardian in each case, 50 patients were randomized using a computer-generated schedule, for single-blind treatment with intravenous paracetamol or intravenous tramadol. Inclusion criteria were age 4-12 yr, ASA physical status I or II, and elective adenotonsillectomy. Patients were excluded from the study if they were developmentally delayed, had neurological dysfunction or renal insufficiency and had allergy to any of the study medications.

All patients were premedicated with oral midazolam 0.5 mg $kg^{-1}$ 30 min before the procedure.

Non-invasive electrocardiography (ECG), peripheral oxygen saturation ($SpO_2$), systolic (SAP), diastolic (DAP) and mean (MAP) arterial pressure monitoring were recorded by a Drager Primus Infinity Delta Monitor (Drager Lübeck, Germany) and baseline values were noted for each patient. Neuromuscular monitoring was performed using a peripheral nerve stimulator with acceleration detection (Train of Four (TOF) Watch, Organon SX). Before anesthesia induction in group P (n=25), 15 mg $kg^{-1}$ paracetamol in group T (n= 25) tramadol 1 mg $kg^{-1}$ (together with normal saline 50 mL) were infused in 10 minutes. SAP, DAP, MAP and heart rate (HR) were recorded. For induction 5-7 mg $kg^{-1}$ thiopental and 0.5 mg $kg^{-1}$ rocuronyum were used. When 95% block had been reached in the TOF monitoring, the patients were intubated. Sevoflurane at 1-2% concentration 50% $O_2$/$N_2O$ were used for anesthesia maintenance. After the end of the surgery the inhalation anesthetic was stopped completely and patients had sufficient spontaneous respiration and TOF>90%, they were extubated.

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SAP, DAP, MAP and HR were recorded before the end of the surgery and after the recovery from anesthesia. The time of the anesthesia, surgery and extubation time were recorded. Time to reach >9 of the Aldrete score [7] were recorded (Table 1). When Aldrete score to reach >9, first value ($0^{th}$) of FLACC score [8] were recorded (Table 2).

FLACC scores were recorded by same physician who was blinded to the analgesic drug used, at $15^{th}$, $30^{th}$, $45^{th}$, $60^{th}$, $120^{th}$, $180^{th}$ and $240^{th}$ minute in the PACU and after then in the patient's room. Rescue analgesia with morphine 0.05 mg $kg^{-1}$ i.v. was administered, after operation, for FLACC score >6. Postoperative analgesic requirements (FLACC score >6) and postoperative side effects like nausea, vomiting, shivering and piruritis were noted.

## Statistical Analysis

SPSS (Statistical Package for social Sciences; SAS Institute INC, Cary, NC, USA) for Windows 10.0 was used for analysis of the data. The sample size for the number of the patients of the study groups was n=24, Power 0.80 and α: 0.05 when Δ: 2.2, SD: 2.7 for the FLACC score parameter. In addition to the descriptive statistical methods (mean ± SD), t-test was used for the comparisons among groups. Repeated measures data were analyzed by ANOVA. Differences from the baseline values were analyzed by Bonferroni's method, paired sample t test. $X^2$ test was used for the qualitative parameters. P<0.05 was accepted as significant.

## Results

There were no significant differences regarding patient characteristics, duration of anesthesia, duration of surgery and extubation time, Aldrete score (time to reach >9) between groups (Table 3).

| | 0 | 1 | 2 |
|---|---|---|---|
| **Activity** | Able to move four extremities voluntarily o on command | Able to move two extremities voluntarily or on command | Unable to move extremities voluntarily or on command |
| **Respiration** | Able to breathe deeply and cough freely | Dyspnea or limited breathing | Apnea |
| **Circulation** | Blood pressure ± 20 %of preoperative level | Blood pressure ± 20 % of preoperative level | Blood pressure ± 50 % of preoperative level |
| **Consciousness** | Fully awake | Arousable on calling | Not responding |
| **$O_2$ Saturation** | Able maintain $O_2$ saturation > 92 % on Air | Needs $O_2$ supplement to maintain $O_2$ saturation > 90 % | $O_2$ saturation > 90 % even with $O_2$ supplement |

**Table 1:** Aldrete Score.

| | 1 | 2 | 3 |
|---|---|---|---|
| **Face** | No particular expression or smile | Occasional grimace or frown, withdrawn, disinterested | Frequent to constant quivering chin, clenched jaw |
| **Legs** | Normal position or relaxed | Uneasy, restless, tense | Kicking, or legs drawn up |
| **Activity** | Lying quietly, normal position, moves easily | Squirming, shifting back and forth, tense | Arched, rigid or jerking |
| **Cry** | No cry (awake or asleep) | Moans or whimpers; occasional complaint | Crying steadily, screams or sobs, frequent complaints |
| **Consolability** | Content, relaxed | Reassured by occasional touching, hugging or being talked to, distractible | Difficult to console or comfort |

**Table 2:** FLACC Score.

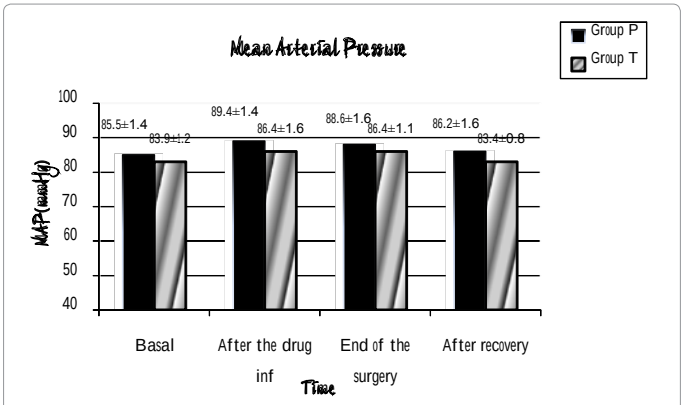


**Figure 1:** Mean arterial pressure.

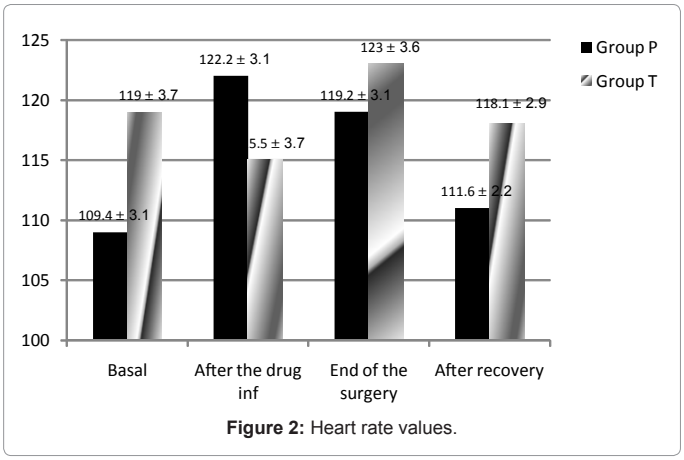


**Figure 2:** Heart rate values.

There was no significant difference in MAP and HR values between groups (Figure 1 and 2).

No significant differences of FLACC score values were found between groups all of the recorded times (Table 4). In the postoperative period no patient needed additional analgesic drug. In the group T vomiting and nausea was observed in four patients (p>0.05) (Table 4).

## Discussion

Pain is the major problem regarding quality of life of children undergoing adenotonsillectomy. Prevention of postoperative pain in children is one of the important objectives of the anesthesiologist. Opioids have been used as an analgesic for postoperative pain in children for many years. Tramadol has both opioid and monoaminergic [9,10]. Recently, an i.v. formulation of paracetamol has been introduced, and its safety and pharmacokinetic properties have been established for children [6].

Preemptive analgesia is based on administration of an analgesic before a painful stimulus generates so as to prevent the subsequent rebound mechanism. The efficiency of preemptive analgesia is evaluated by how much the need of total analgesic is decreased rather than the first analgesic requirement time. Preemptive analgesia gives rise to a subsiding pain pattern, and a decline in morbidity, promoting wellness and shortening the length of hospital stays [11,12].

This is a study to compare the postoperative analgesic effect of preemptive administered i.v paracetamol and i.v. tramadol.

| | Group P (Paracetamol) (n=25) | Group T (Tramadol) (n=25) | P |
|---|---|---|---|
| *Age (Year) | 6.9 ± 2.1 | 7.3 ± 2.5 | 0.199 |
| *Weight (Kg) | 25.3 ± 4.8 | 26.4 ± 5.1 | 0.189 |
| +Gender (F/M) | 11/14 | 12/13 | 0.101 |
| *Duration of anesthesia (min) | 41 ± 14.6 | 43 ± 13.7 | 0.622 |
| *Duration of surgery (min) | 31.2 ± 12.8 | 34.2 ± 13.3 | 0.433 |
| *Extubation time (min) | 5.8 ± 2.9 | 6.4 ± 2.7 | 0.474 |
| *Aldrete score(to reach > 9 min) | 8.8 ± 4.4 | 11.6 ± 4 | 0.307 |

*:*Oneway ANOVA test* +: $X^2$ test

**Table 3:** Demographic properties, duration of anesthesia and surgery, Aldrete core (Mean ± SD).

| | Group P (Paracetamol) (n=25) | Group T (Tramadol) (n=25) | p |
|---|---|---|---|
| *First time (After the Aldrete score to reach < 9) | 3.7 ± 0.4 | 3.8 ± 0.5 | 0.108 |
| *15$^{th}$ min | 3.2 ± 0.4 | 3.2 ± 0.5 | 0.109 |
| *30$^{th}$ min | 1.8 ± 0.3 | 1.8 ± 0.4 | 0.108 |
| *45$^{th}$ min | 1.2 ± 0.3 | 1 ± 0.3 | 0.652 |
| *60$^{th}$ min | 0.5 ± 0.1 | 0.4 ± 0.2 | 0.217 |
| *120$^{th}$ min | 0.4 ± 0.2 | 0.1 ± 0.1 | 0.869 |
| *180$^{th}$ min | 0.04 ± 0 | 0.04 ± 0 | |
| *240$^{th}$ min | 0 | 0 | |
| +Vomiting-Nausea (Patients number) | 0 | 4 | 0.110 |
| +Postoperative rescue analgesia | 0 | 0 | |

*:*Oneway ANOVA test* +: $X^2$ test

**Table 4:** FLACC Score Values and side effects (Mean ± SD).

There are various studies in the literature regarding the usage of preemptive tramadol, but studies with i.v. paracetamol are rare. We could not detect a study comparing preemptive usage of i.v. paracetamol and i.v. tramadol. In papers that tramadol was studied, peroperative i.v. tramadol or peritonsilllary infiltration was shown to be efficient [13,14]. Clinical experience in the use of tramadol reflects mostly paediatric tonsillectomies. Macarone et al. [15], found that tramadol 2 mg $kg^{-1}$ i.v. provided satisfactory intra-operative analgesia in a series of 110 patients aged 4-10. Ozkose et al. [9], evaluated low dosage tramadol (1 and 0.5 mg $kg^{-1}$) and placebo in 45 children undergoing tonsillectomy. It was concluded that low dose tramadol given at induction, provided efficient preemptive analgesia for the intra-and immediate post-operative periods. On the other hand, since tramadol is an opioid it has side effects as nausea, vomiting and elongation of the sedation [16,17].

Although oral administration of paracetamol is very common, i.v. administration is relatively new [18,19]. It was demonstrated that i.v. paracetamol has a faster analgesic effect at early time intervals, a higher effectiveness and a longer analgesic effect than an equivalent paracetamol dosage compared to oral application. Clinical studies have found that 1g i.v. paracetamol employed alone is just as effective as 30 mg ketorolac, 75 mg diclofenac or 10 mg morphine. Studies have also shown that i.v. paracetamol has an opioid-sparing effect and enhances patient satisfaction by reducing the opioid requirement [20,21]. Especially in children preoperative and postoperative oral intake of the drugs may be difficult, and by oral administration elimination time and efficiency time are known to be longer.

In the current literature, we found that 1g paracetamol has been administered preemptively in lumbar disc surgery in three recent publications. In one of these studies, paracetamol 1g IV was administered as additional analgesic to PCA morphine in the postoperative period and provided effective analgesia equivalent to metamizol 1g [22]. Recently, both Toygar et al. [23] and Grundman et al. [24] failed to demonstrate a beneficial preemptive analgesic effect of 1g i.v. paracetamol.

In our study, efficacy of preemptive i.v. parasetamol and i.v. tramadol was compared in children. FLACC score was prefered for the assessment of pain. We thought that activity and consolability could give us reliable knowledge about agitation. In results, we could not detect a significant difference regarding FLACC scores of the groups. None of the patients required additional analgesia.

Vomiting is common after tonsillectomy and may be induced not only by swallowed blood and oropharyngeal irritation but also opioids. Reported gastrointestinal effects of tramadol also include nausea, vomiting and constipation, but to a lesser extent than with opioids [25,26]. In our study, four patients in tramadol group had nause and vomiting this was found to be insignificant statistically.

In conclusion, our findings indicate that preemptively administered i.v. paracetamol 15 mg $kg^{-1}$ or tramadol 1 mg $kg^{-1}$ in children undergoing adenotonsillectomy operation has no negative effects on intraoperative or postoperative hemodynamic parameters, ensures an effective analgesia during the postoperative period.

Preemptive i.v. paracetamol and tramadol were found to be efficient preemptive analgesics in adenotonsillectomy of children for postoperative analgesia.

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