

# EFFICACY OF PERITONSILLAR INFILTRATION OF KETAMINE, TRAMADOL, AND LIDOCAINE FOR PREVENTION OF POST TONSILLECTOMY PAIN

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## ABSTRACT

**BACKGROUNDS:** Tonsillectomy is one of the most common surgeries in children. Controlling pain after tonsillectomy is still controversial. In this study, the efficacy of peritonsillar injection of lidocaine, tramadol, ketamine, and placebo is compared on post tonsillectomy pain.

**METHODS:** In a randomized double-blind clinical trial, 120 patients referring for tonsillectomy to Imam Khomeini hospital in Ahvaz, Iran were recruited into four groups: ketamine, tramadol, lidocaine, and normal saline. One milliliter of medications was injected in each tonsil. Surgery was performed by a surgeon with sharp dissection technique without electrocautery. Pain was recorded 1, 4, 8, 16, and 24 hour(s) after the operation.

**RESULTS:** Baseline characteristics such as age, sex, weight, height, and surgery and anesthesia time did not differ significantly among four groups. Pain scores decreased over time in all groups. No significant difference was observed among ketamine, tramadol, lidocaine, and placebo regarding pain quantity, surgery time, the first time of analgesic requirement, hospital stay, and beginning liquid diet.

**CONCLUSION:** Local injection of ketamine, tramadol, and lidocaine were not significantly different from placebo for prevention of pain in the first 24 hours after tonsillectomy.

**KEYWORDS:** Tonsillectomy, pain, lidocaine, tramadol, ketamine

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## INTRODUCTION

**T**onsillectomy is one of the most common surgeries in children that is followed by severe and significant postsurgical pain, which not only affects the patients' health negatively, but may also cause swallowing dysfunction, bleeding, and dehydration. Despite the emphasis on controlling pain after tonsillectomy, nearly 50% of children undergoing this procedure experience severe pain after the surgery<sup>(1)</sup>.

Pain after tonsillectomy is not only a pathophysiologic matter, but also affects the patient's quality of life.

Controlling patients' pain reduces recovery and hospitalization time. Surgery causes tissue damage and release of biochemical substances such as prostaglandins and histamine, which transmit pain messages to the central nervous system by stimulating nociceptors. Neuro-endocrine response to pain causes hypercoagulation state, immune suppression, and hypoglycemia, which cause a delay in wound recovery<sup>(2)</sup>. Pain after tonsillectomy is usually treated by narcotics that increase the risk of respiratory depression after surgery. Dexamethasone and other steroids are also associated with complications like adrenal gland suppression<sup>(2)</sup>.

Pain after tonsillectomy is still a controversial topic. Local methods of pain control have the advantage of tolerability by patient<sup>(3)</sup>.

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Several studies have suggested topical peritonsillar administration of analgesics and anesthetics to reduce pain after tonsillectomy and have reported different results on the quality and duration of analgesia<sup>(4,5)</sup>.

Tramadol is a  $\mu$ 1, noradrenergic, and serotonergic agonist. In addition to the systemic effect, the local analgesic effect of tramadol on peripheral nerves has been shown in laboratory and clinical studies<sup>(6)</sup>.

Ketamine is an NMDA antagonist receptor and blocks pain messages to the limbic system by blocking glutamate receptors of brain's thalamus. It can be administered through intravenous, intramuscular, rectal, epidural, and intranasal pathways. Different studies have shown effects of sub-analgesic doses of ketamine on postoperative pain and opioid consumption<sup>(2)</sup>.

Lidocaine is a topical amide-like analgesic. It is locally injected in multiple procedures. A vasoconstrictor like adrenaline is usually added to reduce its absorption by local blood flow and reduce bleeding<sup>(7)</sup>.

In this study, we compare peritonsillar injection of lidocaine, tramadol, ketamine, and placebo on post tonsillectomy pain.

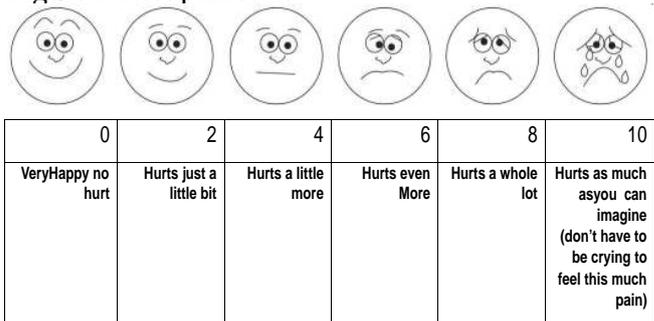
#### MATERIALS AND METHODS:

The current study is a randomized three blinded clinical trial (IRCT code: IRCT2014121520320n1). After permission from the Ethics committee of the Ahvaz University of Medical Sciences, Iran (Ethics code: Ajums. REC.1393.346), 120 patients referring for tonsillectomy to Imam Khomeini hospital, Ahvaz in 2014 who were between 4 and 15 years were enrolled. Written consent to participate in the research was obtained from all parents. Patients with chronic tonsillitis were recruited. Exclusion criteria included patients with underlying diseases or known physiologic problem, patients with a history of drug sensitivity to anesthetic drugs or studied drugs, patients whose surgery took more than one hour<sup>(4)</sup>. General anesthesia was equally induced with 3  $\mu$ g/kg fentanyl, 5 mg/kg STP, 0.5 mg/kg atracurium, 0.02 mg/kg atropine, and 0.03 mg/kg midazolam and then tracheal intubation was performed. Patients were randomly divided into four groups: the first group received 0.5 mg/kg ketamine (Rotexmedica, TriTTAU, Germany), the second group 2 mg/kg tramadol (Daroupakhsh, Iran), the third group 20 mg/ml lidocaine hydrochloride (Daroupakhsh, Iran) and epinephrine 0.00125%, and the fourth group received 2ml normal saline. 2 cc of drugs were prepared and 1 cc was injected in anterior pillar of each tonsil before tonsillectomy. All Surgeries were performed by one

surgeon with sharp dissection technique without electrocautery. In the end of the procedure, anesthesia was reversed with muscle relaxants: 0.05 mg/kg neostigmine and 0.02 mg/kg atropine. Pain was recorded 1, 4, 8, 16, and 24 hour(s) after the operation. The surgeon, the evaluator (ear, nose and throat assistant), and patients were unaware of the drug type. The extubation time was considered zero. The pain was measured with the faces pain scale (Figure 1). This method includes 6 smiling to crying faces and the patients were asked to express their feeling about the similarity of these faces to themselves after surgery and they got a score according to the selected face. When pain was more than 4, 0.5 cc/kg acetaminophen syrup was prescribed<sup>(2)</sup>. The time of the first request for analgesic, the total amount of consumed analgesic, and starting the liquid diet were recorded.

Descriptive statistics was used to estimate mean, standard deviation, and plotting graphs. To analyze and compare the effects of drugs on normal distribution of data, variance analysis or its non-parametric equivalent was used. The chi-square test was also used to analyze qualitative variables.

Figure 1- faces pain scale



#### Results:

The demographic information of patients, duration of surgery and anesthesia are presented in table 1. No significant difference was observed among four groups regarding demographic data (age, sex, weight, and height), and duration of surgery and anesthesia.

Table 1. Demographic and surgical characteristics of patients

variables	Lidocaine	Ketamine	Tramadol	Placebo	Pvalue
Age (mean $\pm$ SD,year)	8.53 $\pm$ 3.2	9.23 $\pm$ 2.4	8.5 $\pm$ 2.9	7.4 $\pm$ 1.9	0.07
Gender(Male)	26.7%	36.7%	26.7%	46.7%	0.3
Weight(Kg)	34.37 $\pm$ 16.8	31.3 $\pm$ 11.3	33.16 $\pm$ 14.8	27.7 $\pm$ 7.4	0.23
Height(Cm)	129 $\pm$ 20.7	129 $\pm$ 13.3	128.8 $\pm$ 20.25	125 $\pm$ 11.3	0.79
Surgery time	24.1 $\pm$ 12.6	28.3 $\pm$ 11.9	24.13 $\pm$ 12.6	30.2 $\pm$ 11.7	0.14
Anesthesia time	46.6 $\pm$ 10.36	44.3 $\pm$ 11.1	46.7 $\pm$ 10.4	45.2 $\pm$ 13.7	0.82

No significant difference was found among groups regarding length of hospital stay, and time of first

analgesic request, the consumed amount of analgesic, and time of liquid diet start (Table 2).

Table 2. The first request for analgesic, consumed amount of analgesic, length of hospital stay, and time of liquid diet start (mean  $\pm$  SD)

variables	Lidocaine	Ketamine	Tramadol	Placebo	Pvalue
Analgesic time(hour)	1.86 $\pm$ 3.1	2.26 $\pm$ 3.3	1.87 $\pm$ 3	0.93 $\pm$ 2.45	1.07
Analgesic amount(dose)	0.37 $\pm$ 0.61	0.4 $\pm$ 0.62	0.36 $\pm$ 0.61	0.4 $\pm$ 0.77	0.02
Hospitalization(hour)	17.2 $\pm$ 6.04	18 $\pm$ 6.1	21.2 $\pm$ 10.7	18.8 $\pm$ 6.04	0.19
PO time(hour)	5.7 $\pm$ 0.46	5.7 $\pm$ 0.62	5.7 $\pm$ 0.47	6.07 $\pm$ 0.74	0.05

Information about the frequency of pain during the first 24 hours after surgery is presented in table 3. No significant difference was seen among groups regarding pain score.

Table 3. Pain score after tonsillectomy in four groups (mean  $\pm$  standard deviations)

Post operation pain	Lidocaine	Ketamine	Tramadol	Placebo	Pvalue
1 hour	7.04 $\pm$ 2.9	-	6.4 $\pm$ 2.5	4 $\pm$ 2.45	0.089
4 hour	6.6 $\pm$ 2.78	5.68 $\pm$ 3.4	5.7 $\pm$ 2.4	5.2 $\pm$ 3.2	0.4
8 hour	5.53 $\pm$ 3.35	4.6 $\pm$ 2.6	4.2 $\pm$ 2.4	4.5 $\pm$ 2.9	0.31
16 hour	2.6 $\pm$ 2.3	3.5 $\pm$ 2.5	2.4 $\pm$ 2.1	2.2 $\pm$ 2.4	0.16
24 hour	1.4 $\pm$ 1.4	2.6 $\pm$ 2.58	1.4 $\pm$ 1.4	1.6 $\pm$ 2.35	0.07

## DISCUSSION

In this study, the effect of local injection of ketamine, tramadol, and lidocaine was compared on pain prevention after tonsillectomy. 120 patients referring for tonsillectomy to Imam Khomeini hospital, Ahvaz, in 2014 between 4 and 15 years old were enrolled. Four groups of 30 participants randomly received ketamine, tramadol, lidocaine, and normal saline. Pain scores decreased in all groups over time.

Tekelioglu UY and colleagues showed in a study in 2013 entitled "Comparison of topical tramadol and ketamine in pain treatment after tonsillectomy." that topical ketamine and tramadol were equally effective in pain relief after tonsillectomy.<sup>(8)</sup>

Heiba MH et al's study in 2012 entitled "Comparison of peritonsillar infiltration of tramadol and lidocaine for pain relief after tonsillectomy" demonstrated that peritonsillar infiltration of tramadol was more effective than lidocaine for pain relief in the first six hours after surgery.<sup>(4)</sup>

Ayatollahi V and colleagues showed in a study in 2012 entitled "Comparison of peritonsillar injection of ketamine and tramadol on pain after tonsillectomy" that tramadol had significantly less pain, longer time to first analgesic request, less time to start the liquid diet, better hemodynamic parameters such as blood

pressure and heart rate than the other two groups. Ketamine had significantly more negative behavior and delusion than the other two groups<sup>(2)</sup>.

In Akbay BK et al's study, pain was significantly lower in tramadol group, but other parameters (nausea, vomiting, fever, constipation, abdominal pain, sore throat, painful swallowing, ear pain, trismus, and halitosis) were not significantly different<sup>(3)</sup>.

In another study by Akkaya T et al entitled "Comparison of peritonsillar and intravenous injection of tramadol for pain relief in children after adenotonsillectomy" that peritonsillar administration of tramadol was more effective for pain relief<sup>(9)</sup>.

In the study by Bushra Abdul Hadi and Saleh M. Sbeitan in 2015 entitled "Clinical pharmacy intervention post tonsillectomy: a randomized control trial." 60 cases of 7-12 years old patients undergoing tonsillectomy were divided into two groups: the first group received peritonsillar infiltration of tramadol and ketamine, and the second group received peritonsillar infiltration of tramadol and ketamine. The second group had less pain. The amount of analgesics required, surgery time, and PONV were similar in both groups<sup>(10)</sup>.

In our study, no significant difference was observed between ketamine, tramadol, lidocaine, and placebo regarding pain volume, surgery time, time of first analgesic request, hospital stay, and time of liquid diet start.

The limitation of this study was the pain measurement scale, in which people's response and understanding is very diverse and also that the studied population was children whose responses to these questions were unreliable.

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