Comparison of Effects of Peritonsillar Infiltration of Tramadol and Lidocaine in Relief of Post-tonsillectomy Pain

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Comment [R11]: A very well conducted and presented RCT. Publication is recommended once some minor changes have been made to the figures. See comments in the uploaded version.
ABSTRACT:

Background:
Peritonsillar infiltrations of local anesthetics and/or locally active analgesic drugs have been used in several studies for relief of post-tonsillectomy pain with variable results in quality and duration of analgesia.

Aim:
To compare the effects of peritonsillar infiltration of lidocaine versus tramadol or placebo on postoperative pain after tonsillectomy.

Methods:
Sixty patients, ASA physical status I–II, aged above ten years, undergoing bilateral elective tonsillectomy under general anaesthesia, were randomized into three groups to receive peritonsillar infiltration after tonsillectomy was performed:
- Group (T) received 2 mg × kg⁻¹ tramadol.
- Group (L) received 2 mg × kg⁻¹ lidocaine 2%.
- Group (S) received 8 ml normal saline only, before tracheal extubation.

The patients in each group were compared postoperatively with regard to the quality of pain control using the visual analogue scale (VAS), and their analgesic requirements.

Results:
Peritonsillar infiltration of tramadol provided analgesic effect in the first 6 postoperative hours comparable to that of lidocaine as reflected by lower recovery room VAS pain scores than that of placebo group (P < 0.05) and also
for opioid requirements (P < 0.01). VAS pain scores and analgesic requirements were similar among the two groups (T) and (L).

**Conclusions:**
Peritonsillar infiltration of tramadol 2 mg × kg⁻¹ provides post-tonsillectomy pain control in the first 6 postoperative hours comparable to that of lidocaine 2 mg × kg⁻¹.

**Key words:** Post-tonsillectomy Pain, Peritonsillar Infiltration, Lidocaine, Tramadol.
Introduction:

Tonsillectomy is one of the most commonly performed operations, and pain after tonsillectomy still remains to be a frequent and frustrating problem \[1\], which can affect the duration of inpatient care, analgesic consumption, oral intake, ambulation, and return to regular activity \[2\]. Relief of pain after tonsillectomy is thus a major concern in order to improve the patient quality of life in the postoperative period \[3\].

The oropharynx and the tonsillar fossae are exquisitely sensitive. They are well innervated locally by the branches of the trigeminal and glossopharyngeal nerves and are highly represented in the somatic cerebral cortex \[4\].

Many treatment modalities for post-tonsillectomy pain have been used, ranging from systemic opioids to different surgical techniques, even radiation \[5\]. Because of the absence of any respiratory depressant effect, there has been a renewed interest in local anesthetic techniques as an effective means of postoperative pain control \[4\].

A previous study utilizing lidocaine 1% topical spray, 4 mg × kg⁻¹ evenly distributed on the tonsillar beds, showed considerable improvement in pain scores in the immediate postoperative period after tonsillectomy when compared with codeine 1.5 mg × kg⁻¹ im \[6\].
Tramadol is a centrally-acting drug, which is effective in the treatment of moderate to severe pain \(^7\). In addition to its systemic action, the local anesthetic effect of tramadol on peripheral nerves has been shown in both laboratory and clinical studies\(^8,9\).

In a previous study \(^10\), it was demonstrated that peritonsillar infiltration with tramadol improves pediatric tonsillectomy pain.

The analgesic effect of peritonsillar infiltration of lidocaine and tramadol in relief of post-tonsillectomy pain has been evaluated in a few studies only, and there is no comparative study between these two drugs in this route of administration.

The aim of this study was to compare the effect of peritonsillar infiltration of lidocaine versus tramadol or placebo on postoperative pain after tonsillectomy.
Patients and methods:

In a double-blind, randomized study, we studied 60 healthy patients, ASA physical status I–II, aged between 12-20 years, undergoing bilateral elective tonsillectomy. Patients with hepatic or renal disease, a history of drug or alcohol abuse, chronic pain states or daily intake of opioids were excluded.

Informed parental or patient consent was obtained from all patients, and the study was approved by the local Ethics Committee.

All patients were instructed preoperatively in the use of the 100 mm Visual Analogue Scale (VAS) for pain (0 = no pain to 100 = the worst pain) [1].

All patients were fasted and unpremedicated. Routine monitoring devices (ECG, non invasive blood pressure cuff, oxygen saturation monitor, and end-tidal CO2) were used. Induction of anesthesia was performed with IV administration of atropine 0.02 mg × kg-1, thiopentone 5 mg × kg-1 and fentanyl 1 μg × kg-1. Succinylcholine 1 mg × kg-1 was used to facilitate tracheal intubation. Anesthesia was maintained with 60% nitrous oxide to oxygen and isoflurane. All patients were allowed to breathe spontaneously throughout the surgical procedure.
All tonsillectomies were performed using the same blunt dissection technique (Boyle–Davies). At completion of the tonsillectomy and after hemostasis using bipolar diathermy was achieved, and for peritonsillar infiltration, patients were randomly allocated by means of (closed envelope) to one of three groups (n=20):

**Group (T)** received 2 mg × kg⁻¹ tramadol in 8 ml of normal saline (4 ml per tonsil);

**Group (L)** received 2 mg × kg⁻¹ lidocaine 2% in 8 ml of normal saline,

In both groups, the injection volume was 8 mL containing 1/200,000 adrenalin, and;

**Group (S)** received 8 ml normal saline only, before tracheal extubation.

The infiltration solution was prepared in a room separate from the surgical suite and only the attending anesthetist knew what solution was administered. The volume of solution given was similar in each group.

The tonsillar bed and peritonsillar tissues on both sides were infiltrated using the same technique, with fan–wise injections from the superior and inferior poles of the fossa. The investigator responsible for the infiltration had no contact with the patients in the postoperative period.

All patients had their tracheas extubated when awake and with intact gag reflex and were transferred to the post-anesthesia care unit (PACU), and observed by nursing staff that was unaware of the treatment that each had received.
Assessments were performed at the time of admission, at 30 min, and immediately before discharge from PACU to the ward. Visual analogue scales were requested from patients when they were awake. The pain assessments were continued on the ward every hour for 6 hours postoperatively.

Postoperative supplementary analgesic was available to the patients in the form of meperidine 1mg × kg-1 was administered iv if the recorded VAS score was 50 or greater.

Bearable pain period of time was considered as the time from full recovery to the first requirement of meperidine. The total meperidine consumption during the first 6 hours was recorded. No other analgesics were administered.

The occurrence of side effects such as hypotension, bradycardia, nausea, vomiting, sedation, or other side effects was recorded for each patient at the same time points as those defined for VAS assessment.

**Statistical analysis:**

Data were analyzed using computer statistical software system SPSS version 12.0 (SPSS Inc., Chicago, IL, USA). Patient characteristics data, operative time and time delay between peritonsillar infiltration and supplementary analgesic administration were analyzed using two-tailed unpaired t-tests. Differences in pain scores and total meperidine consumption between groups were analyzed using repeated-measures analysis of variance (ANOVA) to compare changes within each group. The results were reported as mean values ± standard deviations (SD). P < 0.05 was accepted as statistically significant.
Results:

As regards the demographic characteristics, there were no significant differences in the mean age, weight of patients, sex distribution, and ASA physical status, and duration of surgery among the three groups as seen in Table (1).

Postoperatively, pain scores (Figure 1) were significantly higher in the saline group than in the other two groups ($P < 0.05$). But, groups T and L had comparable pain scores that were statistically non significant ($P > 0.05$).

The time to first postoperative analgesic request was longer in the T and L groups versus control S group; as it was (134 ±18 min) for T group, (135 ± 15
(34 ±11 min) (P < 0.01) (Figure 2).

Supplementary analgesic consumption during the first 6 h was almost equivalent for the T and L groups as five patients in T group and seven patients in L group received one dose each of meperidine (mean consumption of 35 ± 11 and 33 ± 15 mg respectively) which were statistically non significant (P > 0.05). However, supplementary analgesic consumption was greater in S group where mean meperidine consumption during the first 6 h was 75 ± 14 mg (P<0.01) (Figure 3).

No side-effects were reported during the first 6 hours after surgery. Heart rate and arterial pressure did not change significantly. No patient complained of nausea, vomiting, sedation or other side effects.

Discussion:

Postoperative pain and its sequelae are amongst universal complaints of the patients, and post-tonsillectomy pain remains a considerable clinical problem.

This study shows that post-tonsillectomy infiltration of tramadol 2 mg × kg⁻¹ or lidocaine 2 mg × kg⁻¹ in 8 ml of normal saline (4 ml per tonsil); containing 1/200,000 adrenalin, reduces immediate postoperative pain in patients compared with placebo.
Although the use of IV meperidine was less in the tramadol and lidocaine infiltration groups, pain scores after about four hours, were higher than 50 which required the administration of supplementary analgesia according to study protocol. This would suggest that the clinical analgesic effect of the infiltrated tramadol or lidocaine after tonsillectomy is limited to about four hours, after which time, pain assessment may have become unreliable because it will be affected by the systemic analgesia.

Our findings are in agreement with results from a previous study\cite{10}, where peritonsillar infiltration of tramadol in pediatric patients provided superior postoperative analgesia to placebo for 4 hours after surgery. In addition, in that study, tramadol group received significantly more doses of paracetamol than placebo group in order to maintain analgesia in the first 12 hours after recovery from anesthesia\cite{10}.

In another study comparing the postoperative analgesic effect of tramadol versus lidocaine when used as subcutaneous local anesthetic\cite{12}, it was found that the duration of postoperative analgesia provided by subcutaneous tramadol was significantly longer when compared with lidocaine injection (group T $4.9 \pm 0.3$, group L $4.4 \pm 0.7$ hours). Additionally, in that study, the total amount of the consumed analgesic in the postoperative period was considerably less in group T\cite{12}.

Tramadol was thought to produce its antinoceptive and analgesic effects through spinal and supraspinal sites rather than via a local anesthetic action.
However, several clinical studies have shown that tramadol might have peripheral local anesthetic effect \cite{9, 12}. By direct tramadol application to the sciatic nerve in rats, it was proven that tramadol exerts a local anesthetic effect \cite{7}.

In the present study, tramadol had a local anesthetic action similar to that of lidocaine, and because of its antinociceptive effect, it could extend the postoperative pain-free period.

When extracellular sodium concentration decreases, the nerve fiber becomes sensitive to local anesthetics \cite{13}. Jou et al. \cite{8} suggested 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. However, Mert et al. \cite{14} proposed that tramadol might have a mechanism different from that of lidocaine for producing conduction blocks; the presence of a large Ca+2 concentration in the external medium increases tramadol's activity whereas decreasing lidocaine's activity.

Akbay et al. \cite{15} studied the effects of topical tramadol on postoperative pain and morbidity in children undergoing tonsillectomy, and concluded that topical 5% tramadol with its local anesthetic effect seems to be an easy, safe, and comfortable approach for pain management in children undergoing tonsillectomy.

In another study \cite{16} to investigate the efficacy of intramuscular injection and peritonsillar infiltration of tramadol to prevent pain in children undergoing tonsillectomy, it was concluded that peritonsillar infiltration with tramadol
provided good intraoperative analgesia, less postoperative pain on awakening and lower analgesic requirement within the first hour after surgery.

Nausea and vomiting have been major side effects of tramadol used for postoperative analgesia. The incidence of these side effects seems to be related mainly to the peak serum concentrations, as an initial IV loading dose of 3 mg/kg caused more symptoms than a subsequent infusion or patient-controlled analgesia \(^{[17]}\).

In a study \(^{[18]}\) comparing the postoperative analgesic efficacy and side-effects of IV tramadol with peritonsillar infiltration of tramadol in children undergoing adenotonsillectomy, it has been demonstrated that peritonsillar infiltration of tramadol maintains efficient pain relief with lower incidence of nausea and vomiting in comparison to IV administration.

Summary

- With peritonsillar infiltration of tramadol, the postoperative pain-free periods were significantly prolonged
- With peritonsillar infiltration of tramadol less analgesic were required
- These effects are comparable to the analgesic effects of lidocaine 2 mg × kg\(^{-1}\).
- Peritonsillar infiltration of tramadol 2 mg × kg\(^{-1}\) provides post-tonsillectomy pain control in the first 6 postoperative hours comparable to that of lidocaine 2 mg × kg\(^{-1}\).
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Results:

(Table 1): Demographic data of the three groups (mean ± SD):

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group T (n=20)</th>
<th>Group L (n=20)</th>
<th>Group S (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>15.3 ± 2.2</td>
<td>14.9 ± 2.5</td>
<td>15.2 ± 2.3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>38.2 ± 3.1</td>
<td>37.3 ± 3.2</td>
<td>38.1 ± 3.1</td>
</tr>
<tr>
<td>Male/female</td>
<td>11/9</td>
<td>10/10</td>
<td>12/8</td>
</tr>
<tr>
<td>ASA class I/II</td>
<td>13/7</td>
<td>14/6</td>
<td>12/8</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>27 ± 9</td>
<td>30 ± 4</td>
<td>29 ± 5</td>
</tr>
</tbody>
</table>

No significant difference between the three groups. T= Tramadol, L= Lidocaine, S= Saline.
(Figure 1): Visual Analogue Scale (VAS) after tonsillectomy in the three groups (mean).
\( T = \text{Tramadol}, \ L = \text{Lidocaine}, \ S = \text{Saline} \).

(Figure 2): Time to first analgesic request after tonsillectomy in the three groups (mean).
\( T = \text{Tramadol}, \ L = \text{Lidocaine}, \ S = \text{Saline} \).
(Figure 3): Mean Dose of Meperidine Consumption during the first 6 h after tonsillectomy in the three groups (mean). T = Tramadol, L = Lidocaine, S = Saline.