Comparison of Post-Operative Analgesic Effects of Peritonsillar Infiltration of Dexmedetomidine, Lidocaine or Both in Children Following Tonsillectomy

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ABSTRACT

Background: Peritonsillar infiltration of local anesthetics has efficient pain relief in children undergoing tonsillectomy. We hypothesize that lidocaine plus dexmedetomidine will potentiate the analgesic effect of each other rather than.

Objectives: This study aimed to compare the analgesic effect of peritonsillar infiltration of lidocaine, dexmedetomidine, or lidocaine/dexmedetomidine on post-tonsillectomy pain. The primary outcome is the time of analgesia. The secondary outcomes are postoperative pain score, the effect of study medications on postoperative hemodynamic, and complications.

Patients and Methods: Ninety patients were randomly allocated to three groups, 30 patients each. L group, patients received 2mg/kg lidocaine. D group, patients received 1 μg/kg of dexmedetomidine. LD group, patients received 1 μg/kg of dexmedetomidine plus 2 mg/kg lidocaine.

Results: The time of the first analgesia request (h.) was longer in the LD group (13.70 ± 2.91) when compared with the L and D groups. Postoperative pain score was significantly lower in LD and D groups compared with the L group (P <0.05) On the other hand, there was a significantly lower median VAS score in the LD group when compared with the D group (P1 <0.05) Postoperative paracetamol consumption was significantly lower in LD group (0.55 ± 0.51 gm/24h) when compared with D and L groups (0.65 ± 0.59, 2.25 ± 0.44 gm/24h respectively).

Conclusion: The use of lidocaine with dexmedetomidine is better than using each drug alone in decreasing post-tonsillectomy pain and increasing the time to first request for analgesia with no significant postoperative side effects.

Keywords: Posttonsillectomy pain, Lidocaine, Dexmedetomidine.

INTRODUCTION

Tonsillectomy with or without adenoidectomy remains one of the most commonly performed surgical procedures in pediatrics. The main complications of this surgery are hemorrhage, pain, nausea, vomiting, and dehydration (1). In an attempt to decrease complications, a wide spectrum of surgical techniques for tonsillectomy has been developed. Additionally, various perioperative adjuvant therapies such as local anesthetic, steroids, analgesics, antibiotics, and antiemetics have been implemented to improve outcomes (2).

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 well represented in the somatic cerebral cortex (3). A local anesthetic agent administered at the peritonsillar space that provides analgesia with minimal adverse effects is an attractive solution to the problem of post-tonsillectomy pain (4).

Dexmedetomidine is a highly selective α2-adrenoceptor agonist that produces dose-dependent sedation, anxiolysis, and analgesia without respiratory depression (5, 6). The present study has been planned to assess the post-tonsillectomy analgesic efficacy of peritonsillar lidocaine infiltration with dexmedetomidine rather than each drug alone and possible postoperative complications in children undergoing tonsillectomy.

The study aimed to compare the analgesic effect of peritonsillar infiltration of lidocaine, dexmedetomidine, or lidocaine/dexmedetomidine on post-tonsillectomy pain. The primary outcome is comparing between the studied groups regarding the time of analgesia. The secondary outcomes are postoperative pain score, the effect of study medications on heart rate, mean arterial pressure, and postoperative nausea and vomiting (PONV).

PATIENTS AND METHODS

Ethical Considerations:

This randomized double-blind study was performed at Mansoura University Hospitals, Dakahlia, Egypt after being approved by the Institutional Review Board (IRB) with a code number; MS/17.03.36. The study was presented following the Consolidated Standards of Reporting Trials (CONSORT) guidelines. Written informed consent was taken from the child’s parents after explanation of the procedure and purpose of the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Nightly children of either sex with American Society of Anesthesiologists (ASA) physical status I or...
II, aged from 5-15 years scheduled for elective tonsillectomy surgery.

**Exclusion criteria included:** patients with bleeding and coagulation disorders, hepatic and renal diseases, airway problems, patients with cognitive or developmental disorders, patients with a history of known hypersensitivity to the used local anesthetic, and patients who refused to participate in this study.

Eligible ninety patients were randomly divided into three equal groups (30 patients in each), using a closed-envelope method. The patients and the administrator were blinded to the medication administered. The study solutions were prepared by an anesthesiologist who was blinded to the study.

**The three groups according to the study solution were:**

- **Lidocaine group (L group) (n=30):** 2mg/kg lidocaine in 8 ml of normal saline. The injection volume was 8 ml, which contained 1/200 000 adrenaline, 4 ml for each tonsil.

- **Dexmedetomidine group (D group) (n=30):** 1 μg/kg of dexmedetomidine in 8 ml of normal saline. The injection volume was 8 ml, which contained 1/200 000 adrenaline, 4 ml for each tonsil.

- **Dexmedetomidine/lidocaine Group (LD group) (n=30):** 1 μg/kg of dexmedetomidine plus 2mg/kg lidocaine in 8 ml of normal saline. The injection volume was 8 ml, which contained 1/200 000 adrenaline, 4 ml for each tonsil.

All patients were assessed preoperatively by history taking, physical examination, electrocardiogram (ECG), and laboratory evaluation (complete blood count 'CBC', hepatic and renal function tests, coagulation profiles). The day before surgery, all patients were familiar with the use of the visual analog scale (VAS) for pain assessment. The scale consists of 10 cm horizontal line ranging from 0 “no pain” to 10 “worst imaginable pain”. Patients were asked to mark the line vertically at a point that matched their pain. The pain intensity was rated as mild (VAS:0-3), moderate (VAS:4-6), and severe (VAS:7-10) (7). Demographic data as age and sex were registered. In the operating room, patients were monitored with the standard monitoring including an electrocardiogram (ECG), Pulse oximeter (SpO2), and noninvasive arterial blood pressure. Anesthesia was standardized for all patients. General anesthesia was induced with 8% sevoflurane in oxygen through a face mask. After establishing venous access, atracurium 0.5 mg/kg was given. Orotracheal intubation was performed and anesthesia was maintained with 2-3% sevoflurane in oxygen/air mixture and the patients were mechanically ventilated to keep end-tidal CO2 (ETCO2) around 35 mmHg.

Hemodynamic changes (heart rate and mean blood pressure) and oxygen saturation was recorded basely then every 5 min intraoperatively. Sevoflurane concentration was increased if the heart rate or the mean blood pressure increased 20 % above the basal value. All patients received calculated balanced crystalloid solution (Glucose 5% / Ringer) according to their body weight and 0.2 mg/kg IV dexamethasone to decrease upper airway edema. All children were operated on by the same surgical team using sharp dissection technique with snare method and achieving homeostasis with ligatures. After bilateral tonsillectomy, the study solution according to the randomization was injected into the tonsillar bed on both sides (4 ml for each side) in fanwise injections in the upper and lateral parts of the peritonsillar area after aspiration by the surgeon using a straight 25- G needle. At the end of the surgery, sevoflurane was discontinued, residual muscle relaxation was reversed with neostigmine 0.04 mg/kg and atropine 0.02 mg/kg IV.

The oropharynx was suctioned and extubation was performed when the patients were breathing spontaneously with enough tidal volume, their gag reflex was restored and they showed facial grimaces then the patients were transferred to the post-anesthesia care unit (PACU) and followed up for 24 hrs. Anesthesia time (time from the start of induction of anesthesia till extubation), operative time (time from the start of surgery till end of surgery), and extubation time (time from stopping the anesthetics till extubation) were recorded. The patients were transferred to the PACU and pain score was assessed and recorded using (VAS) at (30min,1,2,4,8,16,24 hours) postoperatively.

If pain score ≥ 4, LV paracetamol 15 mg/kg was given as additional analgesia. The time to the first request for supplemental analgesic (the time/hr. from infiltration of study solution until the patient started to ask for analgesia) was recorded. The amount of paracetamol gm/24h was calculated and recorded. The number of patients who asked for analgesia in the studied groups was recorded. Heart rate and mean blood pressure were monitored and recorded preoperatively (basal), post-induction of GA, post-operative time (time from stopping the anesthetics till extubation), and at early post-operative time.

PONV was assessed using Apfel score where; no nausea or vomiting = 0, Nausea without vomiting = 1, One attack of vomiting = 2, More than 1 attack of vomiting = 3. rescue dose of Metoclopramide 0.1 mg/kg was administrated IV if the score was ≥ 1(8). Other complications like edema at the site of injection, arrhythmia, allergic reaction, and secondary hemorrhage were assessed and recorded.

**Sample size calculation and statistical analysis:**

G*Power software version 3.1.9.2 was used for sample size calculation based on the previously published result (5) about the time to first request
analgesia as the primary outcome. Accepting a 35% increase in analgesic time as an accepted effect size, a total sample size of 81 patients was found to be sufficient to achieve a study power of 80% with an alpha error of 0.05.

**Statistical methods:**

A drop out of 10% of cases was expected therefore 90 patients were required. SPSS software version 20 was used for statistical analysis. Continuous variables were tested for normality of distribution. Normally distributed data were described as mean ±SD while non-normally distributed data were presented as median (interquartile range). Nominal and ordinal variables were described as numbers (percentage). ANOVA test was used to detect statistical differences between the studied groups as appropriate. P-value < 0.05 was considered significant.

**RESULTS**

A total number of ninety patients undergoing elective tonsillectomy were enrolled in this study. Demographic data of the studied groups regarding age, sex, operative time, anesthesia time, and extubation time showed no statistically significant differences between the three groups (Table 1).

**Table (1):** Patient characteristics, operative time (min), anesthesia time (min), and extubation time (min) in the studied groups.

<table>
<thead>
<tr>
<th></th>
<th>D group (n=30)</th>
<th>L group (n=30)</th>
<th>LD group (n=30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>7.71 ± 2.59</td>
<td>7.80 ± 2.54</td>
<td>7.33 ± 2.13</td>
<td>0.878</td>
</tr>
<tr>
<td>Sex:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>19 (63.3)</td>
<td>17 (63.3)</td>
<td>19 (63.3)</td>
<td>0.829</td>
</tr>
<tr>
<td>Female</td>
<td>11 (36.7)</td>
<td>14 (37.3)</td>
<td>11 (36.7)</td>
<td>0.756</td>
</tr>
<tr>
<td>Operative time (minutes)</td>
<td>46.00 ± 4.76</td>
<td>45.65 ± 4.85</td>
<td>47.50 ± 5.87</td>
<td>0.067</td>
</tr>
<tr>
<td>Anesthesia time (minutes)</td>
<td>54.75 ± 5.91</td>
<td>53.75 ± 5.50</td>
<td>55.25 ± 5.10</td>
<td>0.074</td>
</tr>
<tr>
<td>Extubation time (minutes)</td>
<td>5.80 ± 0.91</td>
<td>5.90 ± 1.07</td>
<td>5.85 ± 1.31</td>
<td>0.082</td>
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</tbody>
</table>

Table (2): The time to the first request for analgesia (hours), Total paracetamol (gm/24h) consumption, Number of patients who asked for analgesia postoperatively in the studied groups.

<table>
<thead>
<tr>
<th></th>
<th>D group (n=30)</th>
<th>L group (n=30)</th>
<th>LD group (n=30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of first analgesia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>request (h)</td>
<td>5.20 ± 1.03</td>
<td>2.67 ± 0.99</td>
<td>13.70 ± 2.91</td>
<td>P1=&lt;0.001* P2=&lt;0.001* P3=&lt;0.001*</td>
</tr>
<tr>
<td>Paracetamol (g/24h)</td>
<td>2.25 ± 0.44</td>
<td>0.65 ± 0.59</td>
<td>0.55 ± 0.51</td>
<td>P1&lt;0.001* P2&lt;0.001* P3&lt;0.001*</td>
</tr>
<tr>
<td>Patients asked for</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>analgesia (n)</td>
<td>27 (90.0%)</td>
<td>28 (93.3%)</td>
<td>4 (13.3%)</td>
<td>P1=0.526 P2&lt;0.001* P3&lt;0.001*</td>
</tr>
</tbody>
</table>

Data are expressed in mean ± SD, number (percentage) P1=D Vs. L, P2=D vs. LD, P3=L vs. LD * P < 0.05 is considered significant D: dexmedetomidine group, L: lidocaine group, LD: lidocaine dexmedetomidine group, n=number
Perioperative HR was statistically significantly lower in the LD group compared with the D and L groups only at the early postoperative time (108.05 ± 9.27 vs 122.55±3.69 & 118.00±3.42 respectively) (p-value 0.024 & 0.042 respectively) (Table 3).

Table (3): Perioperative HR (beats/min) in the studied groups.

<table>
<thead>
<tr>
<th></th>
<th>D group (n:30)</th>
<th>L group (n:30)</th>
<th>LD group (n:30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal HR (beats/min)</td>
<td>132.25 ±6.44</td>
<td>135.30 ± 5.46</td>
<td>133.90 ± 8.48</td>
<td>P1=0.383, P2=0.342, P3=0.714</td>
</tr>
<tr>
<td>Post-induction HR (beats/min)</td>
<td>133.03 ±8.07</td>
<td>128.97±11.03</td>
<td>128.77 ± 13.01</td>
<td>P1=0.152, P2=0.133, P3=0.943</td>
</tr>
<tr>
<td>Post-injection HR (beats/min)</td>
<td>104.47 ±6.90</td>
<td>106.03±12.93</td>
<td>108.07 ± 13.01</td>
<td>P1=0.593, P2=0.221, P3=0.488</td>
</tr>
<tr>
<td>Early postoperative HR (beats/min)</td>
<td>122.55±3.69</td>
<td>118.00±3.42</td>
<td>108.05 ±9.27</td>
<td>P1=0.035*, P2=0.024*, P3=0.042*</td>
</tr>
</tbody>
</table>

Data are expressed as Mean ± SD
P1= D Vs. L, P2= D vs. LD, P3= L vs. LD
*P < 0.05 is considered significant
D: dexmedetomidine group, L: lidocaine group, LD: lidocaine & dexmedetomidine group, n=number, HR: heart rate

Mean blood pressure was statistically significantly lower in the LD group compared with the D and L groups only at the early post-operative time (69.15 ± 3.12 vs 82.90 ± 2.63 & 76.40 ± 2.30 respectively) (p-value 0.034 & 0.013 respectively). Table 3. As regards the PONV score, there was no statistically significant difference between the three groups.
exmedetomidine to bupivacaine in eritonsillar, f PONV significance when it was compared with ore orination of dexmedetomidine and – its action and prolong its post

the postoperative 24hr. decreases postoperative analgesic requirement during

prolongs the duration of postoperative analgesia and found that adding dexmedetomidine to lidocaine combination in infiltration

nee postoperative pain severity, need for analgesics ketamine was more effective in reducing the as well as the need for analgesics in children undergoing reduce the incidence and severity of postoperative pain which was measured by lower

maxillofacial surgeries is more effective in reducing cleft palate repair resulted in a 50% increase in the duration of postoperative analgesia with no significant side effects

In a study done by Mandal and his co-workers, they concluded that pre-incisional perilesional infiltration of a combination of Dexmedetomidine and lignocaine-adrenaline mixture during reconstructive maxillofacial surgeries is more effective in reducing perioperative pain which was measured by lower consumption of propofol and fentanyl (17). As regard hemostasis, Sørensen and his co-workers in a controlled study proved that low-dose peritonsillar injection of lidocaine–adrenaline mixture before tonsillectomy reduces intraoperative blood loss as well as operation time (18). In the current study, peritonsillar infiltration of dexmedetomidine, lidocaine, or their combination has no significant reduction of PONV between the three groups. Akkaya and his colleagues

| Table (4): Perioperative MBP (mmHg) in the studied groups. |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | D group (n:30)  | L group (n:30)  | LD group (n:30) | P-value         |
| Basal           | 94.85 ± 3.77    | 94.30 ± 5.88    | 94.60 ± 4.56    | P1=0.068        |
|                 |                 |                 |                 | P2=0.096        |
|                 |                 |                 |                 | P3=0.124        |
| Post-induction  | 81.70 ± 11.31   | 80.23 ± 14.73   | 76.77 ± 13.10   | P1=0.666*       |
|                 |                 |                 |                 | P2= 0.149       |
|                 |                 |                 |                 | P3= 0.309       |
| Post-injection  | 65.90 ± 10.29   | 63.47 ± 10.48   | 65.07 ± 9.29    | P1=0.350        |
|                 |                 |                 |                 | P2= 0.749       |
|                 |                 |                 |                 | P3= 0.539       |
| Early post-operative | 82.90 ± 2.63   | 76.40 ± 2.30    | 69.15 ± 3.12    | P1=0.027*       |
|                 |                 |                 |                 | P2= 0.034*      |
|                 |                 |                 |                 | P3= 0.013*      |

Data are expressed in Mean ± SD
P1= D Vs. L, P2= D vs. LD, P3= L vs. LD  *P < 0.05 is considered significant
D: dexmedetomidine group, L: lidocaine group, LD: lidocaine & dexmedetomidine group, MBP = mean blood pressure, n=number

DISCUSSION
One of the most serious and common complications of tonsillectomy is post-tonsillectomy pain. Due to the hyperexcitable state during surgery, pain impulses are conducted into the central nervous system even with general anesthesia. Blockage of these impulses by perioperative infiltration of local anesthetic agents theoretically must have a significant analgesic effect (9). Post tonsillectomy pain is treated usually with non-steroidal anti-inflammatory drugs or opioid analgesics, but respiratory depression and postoperative bleeding were major side effects (3).

Peritonsillar infiltration has obvious privilege when compared with intravenous technique as it provides efficient pain relief without side effects in children undergoing tonsillectomy (9). In their study, Khademi and his colleagues (10) demonstrated that preoperative ketamine administration through the intravenous route and peritonsillar infiltration both reduce the incidence and severity of postoperative pain as well as the need for analgesics in children undergoing adenotonsillectomy. Peritonsillar infiltration of ketamine was more effective in reducing the postoperative pain severity, need for analgesics, and need for antiemetics.

In the current study, we compared peritonsillar infiltration of dexmedetomidine and lidocaine combination with infiltration of each drug alone. We found that adding dexmedetomidine to lidocaine prolongs the duration of postoperative analgesia and decreases postoperative analgesic requirement during the postoperative 24hr. Peyvandi and his colleagues proved that peritonsillar infiltration of lidocaine alone has short postoperative analgesic duration and there was no statistical significance when it was compared with the saline group, so it needs another additive to augment its action and prolong its post-operative analgesic time (11).

In agreement with our study, Yoshitomi and his colleagues showed that dexmedetomidine enhances the local anesthetic action and prolongs the duration of the postoperative analgesic effect of lidocaine (12). In a crossover double-blind study, Yamane his colleagues showed that a combination of dexmedetomidine and lidocaine considerably enhances the local anesthetic potency of lidocaine without any major influences on the cardiovascular system when locally injected into the oral mucosa (13). This passes in parallel with Abosedira who proved that the combination of Dexmedetomidine and lidocaine for Bier’s block prolongs the duration of the block and duration of postoperative analgesia (14).

Furthermore, Bharti and his co-workers showed that adding dexmedetomidine to local anesthetics prolonged the duration of supraclavicular brachial plexus block and improved postoperative analgesia (15). Additionally, Obayah and his colleagues found that the addition of dexmedetomidine to bupivacaine in greater palatine nerve blocks in children undergoing cleft palate repair resulted in a 50% increase in the duration of postoperative analgesia with no significant side effects (16).
found that peritonsillar infiltration of tramadol maintains efficient pain relief with a lower incidence of nausea and vomiting in adentonsillectomy surgery (19).

In the current study, no patient developed a complication of injection of local anesthetics in the tonsillar bed, facial nerve paralysis, upper airway obstruction, or vocal cord paralysis. Shlizerman and his colleague reported a case of 4ys child who developed peripheral facial nerve paralysis after perioperative infiltration of bupivacaine. The paralysis was noticed a few minutes after extubation and resolved completely after 8 hours. This was explained by the direct action of the local anesthetic agent on the facial nerve (20).

CONCLUSION
This study concluded that the use of lidocaine with dexmedetomidine was better than using each drug alone in decreasing post-tonsillectomy pain and increasing the time of first analgesic request with no significant postoperative side effect.

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Conflict of interest: Nil.

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