Does Topical Anesthesia Using Aerosolized Lidocaine Inhibit the Superior Laryngeal Nerve Reflex?

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Abstract

Objective. This study was designed to evaluate the effectiveness of topical lidocaine in attenuating the laryngeal reflex and blunting hemodynamic response by inhibition of the superior laryngeal nerve in laryngeal microsurgery, which would be helpful in preventing potential complications.


Setting. Tertiary medical center.

Subjects and Methods. Fifty-four patients requiring glottic and supraglottic laryngeal microsurgery were randomly assigned to 1 of 2 groups, with equal numbers. Before surgery, 10% lidocaine was topically applied to the laryngeal surface of the epiglottis and vocal folds under direct vision in the study group and saline aerosol was applied in the control group. Heart rates, arterial blood pressure, and SPO2 were recorded at baseline, after induction, immediately before and after intubation, during the surgery, and upon extubation. Laryngospasm, agitation, and coughing were recorded during the recovery period.

Results. Heart rates, arterial pressure, and SPO2 did not differ significantly from baseline to postintubation period among the groups. SPO2 values measured similar in the remaining study. Heart rates and blood pressures were slightly decreased in the study group after lidocaine administration, but only blood pressure at pre- and post-extubation was significantly decreased in the study group (P < .05). Also laryngospasm and coughing were not statistically different between the 2 groups. There was an obvious gap between the 2 groups for agitation. Study group agitation was noted significantly lower (P < .05).

Conclusion. These findings indicate that preoperative topical lidocaine application may be helpful in attenuating airway-circulatory reflexes in laryngeal microscopic surgery.

Keywords
superior laryngeal nerve, lidocaine, vagal reflex, laryngeal microsurgery.

Introduction

The larynx is a potent reflexogenic region of the upper airway that is rich in sensory efferents and that elicits various reflexes. The internal branch of the superior laryngeal nerve (ISLN) innervates the larynx from its superior boundaries to the level of the vocal cords where the sensory distribution of the vagus nerve is more abundant.1,2 In fact, studies on the morphology and location of the sensory receptors in the laryngeal mucosa resulted in insufficient and conflicting data. Thus, the laryngeal reflex occurring in response to mechanical stimulations is still a matter of study.1

Although the operation times for laryngeal microsurgery are relatively short, mechanical contact to the laryngeal airway occasionally induces reflex inhibition of breathing, flushing, coughing, bronchospasm, bradycardia, and hypertension in various species.3,4 One of the frequently overlooked risks of laryngeal surgery is cardiac complications, most likely precipitated by stimulation of the deep pressure receptors of the larynx during suspension laryngoscopy. The overall incidence of cardiac complication is nearly 7% in a high-risk group and almost 2% in the group without preoperative history of cardiac disease.5-7

Reflex glottic closure is a dominant and stable reflex produced by the stimulation of the superior laryngeal nerve. Laryngospasm is an exaggeration of this response stimulated

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by the presence of blood, secretions, or surgical debris, particularly during the light plane of anesthesia. Laryngospasm is also more common after upper airway procedures.\textsuperscript{7,8}

Coughing induced by laryngeal microsurgery is thought to be precipitated via irritant receptors, which are rapidly acting and primarily superficially located. These nociceptive stimuli can result in hypertension, tachycardia, increased intracranial pressure, myocardial ischemia, bronchospasm, and surgical bleeding.\textsuperscript{9}

Lidocaine stabilizes the neuronal membrane by inhibiting ionic fluxes required for the initiation and conduction of impulses, thereby affecting local anesthetic action. Lidocaine is characterized by a rapid onset of action (1-5 min) and intermediate duration of efficacy (10-15 min) when used topically.\textsuperscript{10}

We conducted a double-blind placebo-controlled randomized trial to examine the efficacy of superior laryngeal nerve inhibition with topical application of lidocaine before laryngeal microsurgery in the prevention of laryngeal, cardio-vascular, and pulmonary side effects.

**Materials and Methods**

This prospective study was approved by the Ethics Committee of Tepecik Research and Education Hospital. Patients were monitored and surveyed in accordance with the Helsinki Declaration of 1975, as revised in 1983. All patients provided written informed consent before being enrolled in the study.

From May 2007 to April 2011, 54 patients scheduled to undergo laryngeal microsurgery for laryngeal polyp, Reinke’s edema, and laryngeal malignancy (biopsy for T1 glottic-supraglottic tumor) under general anesthesia were enrolled in this study. Exclusion criteria were: age under 20 or age older than 72 years, Standard American Society of Anesthesiologists (ASA) physical status of more than II, >30% above or <20% below ideal body weight, allergies to study drugs, renal or liver disease, and/or any other systemic disease, including diabetes (Figure 1).

ASA monitoring applied, including electrocardiography, noninvasive arterial blood pressure, pulse oximetry, and end-tidal CO2 for all patients. All patients were intubated at the first attempt with 6 mm inner diameter tube. In both groups, anesthesia was induced with propofol (1.5 mg/kg) and mivacurium (0.2 mg/kg). After mask ventilation with sevoflurane 8% in oxygen for 3 minutes, the trachea was intubated. Anesthesia was maintained with sevoflurane. In both groups, 2 mg/kg methylprednisolone was administered intravenously. No narcotic drugs were used.

The lidocaine and saline solutions were put in similar bottles and these bottles were labeled as A and B, respectively. But the surgeon and the anesthesiologist were blind to the content of the bottle. Laryngoscope blade was positioned below the epiglottis. Two puffs of 10% lidocaine solution (10 mg metered spray) or saline solution were infused through the laryngoscope channel with a 20 cm nozzle, onto the laryngeal surface of the epiglottis. Next, the laryngoscope was located just above the vocal folds and 2-puff infusion repeated at both sides while targeting the anterior one-third of the vocal cord. Before surgery, we allowed a 3 minute waiting period to provide adequate penetration of local anesthetic into the airway mucosa for maximal effect. Noninvasive arterial blood pressure, heart rate, and SPO2 were recorded at 8 different time points:

1. baseline (before induction),
2. after induction,
3. immediately before intubation (pre-intubation),
4. immediately after intubation (postintubation),
5. immediately before the surgery (presurgery; before the surgeon began the procedure),
6. immediately after surgery (postsurgery; when the surgeon completed the procedure),
7. immediately before extubation (pre-extubation),
8. immediately after extubation (post-extubation).

The occurrence of laryngospasm that resolved without treatment was also considered as an adverse event. Laryngospasm was graded as none = 1, mild = 2 (spontaneous relief), moderate = 3 (relieved by applying positive pressure through laryngeal mask airway), or severe = 4 (relieved by succinylcholine administration). Coughing was graded as times during 6 minutes of post-extubation period: none = 1, mild = 2 (1-3 coughs), moderate = 3 (4-7 coughs), and severe = 4 (>7 coughs). Agitation was scored on a 4-point scale: 1 = awake and calm, 2 = mild agitated but consolable, 3 = moderate irritable/restless insconsolable agitated, 4 = severely agitated, combative, disoriented, thrashing incontinent.

Statistical analysis was performed using SPSS 15.0 software (SPSS Inc, Chicago, Illinois). Between 2 groups, the demographic data, arterial blood pressure, heart rate, and number of coughs were analyzed using an unpaired t test. Nonparametric data were analyzed using chi-square test and Fisher’s exact test. P < .05 was considered to be statistically significant.

Results
In the study group, 27 patients, of which 9 had a primary diagnosis of polyp(s), 5 had Reinke’s edema, and the remaining 13 had tumors, were anesthetized with lidocaine solution. In the control group, saline solution was applied to 27 patients, of which 15 had a primary diagnosis of polyp(s), 4 had Reinke’s edema, and the remaining 8 had tumors. Characteristics of cases, definition of laryngeal pathologies, and duration of anesthesia and operation are shown in Table 1.

No statistically significant differences were found between the 2 groups regarding gender, age, body mass index, number of smokers and alcohol users, time of intubation-surgery, laryngeal pathologies, and applied surgery. Also, heart rates, SPO2, and systolic-diastolic blood pressures were not altered significantly between 2 groups in the baseline, after induction, pre-intubation, and post-intubation measurements.

Mean heart rates before and after extubation in the study and control groups were 86.34 to 85.32 and 91.66 to 86.59, respectively. Mean SPO2 after extubation was 98.14% in the study group and 98.11% in the control group. Heart rates were slightly decreased after lidocaine anesthesia in the study group, but changes in heart rates and SPO2 between 2 groups were not significantly different (P > .05) (Tables 2, 3).

After the lidocaine application, systolic-diastolic blood pressure was slightly decreased in the study group, but statistically significant decrease was seen in pre- and post-extubation blood pressure (P < .05) in the lidocaine administered group (Table 4).

Laryngospasm was observed in 2 patients of the study group and 1 patient of the control group. All laryngospasms were noted as mild and improved without additional treatment. Coughing rates and severity were higher in the study group. Laryngospasm and coughing were not statistically different between the 2 groups (P > .05). Agitation was
observed in 5 control group patients, versus only 1 in the study group, and the difference was statistically significant ($P < .05$) (Table 5).

**Discussion**

Airway irritation due to suspension laryngoscopy, in addition to surgical stimulation, can lead possible respiratory complications such as cough, stridor, and laryngospasm and can cause hemodynamic change. In our study, topical lidocaine was applied to supraglottic and glottic areas before the laryngeal microsurgery for blunting the laryngeal and cardiovascular response.

Heart rates and arterial pressure responses can be ranked according to the location of the stimulation site in descending order: larynx, trachea and carina, and bronchus. Transient increases in heart rates and mean arterial pressures commonly occur during laryngoscopy, probably originating from the sympathetic nervous system, which are carried by ISLN sensory branch. Rarely, hypotension, severe bradycardia, and possible asystole can occur following laryngoscopy, presumed to be mediated by the vagus nerve. The tip of the laryngoscope blade lifts the laryngeal surface of the epiglottis or supraglottic area during surgery. Vagus nerve stimulation by compression of the laryngoscope generally occurs. Therefore, larynx microsurgery can noted as a vagotonic procedure. Because of the intense vagal stimulation and cardiovascular response to suspension laryngoscopy, operation must be performed with maximum safety and minimum patient discomfort. This should be obtained to lessen the incidence and severity of postoperative laryngospasm, uncontrollable coughing and agitation and also to reduce the incidence and severity of cardiovascular disturbances associated with laryngeal irritation. For this purpose, topical anesthesia of the ISLN is used in our study. The main goal is effective depression of laryngeal reflexes, both vagotonic and sympathetic, without blunting of the intrinsic protective function. Topical lidocaine anesthesia of the oropharynx, larynx, and trachea before laryngoscopy can prevent increases in arterial blood pressure during laryngoscopy and intubation while decreasing the incidence of coughing and laryngospasm
after extubation. In clinical practice, pharynx, larynx, and trachea are usually anesthetized with local anesthetic sprays using various devices, especially in patients with difficult airways. Local anesthetic agents may have detrimental effects on upper airway muscles, which are potent dilators and tensors of the pharyngeal and laryngeal structures. Neural efferents from pressure receptors in the wall of the upper airways also participate in this regulation. Topical anesthesia of the upper airway has been considered to depress the response of these receptors and to disrupt the neural loop, which participates in maintaining the patency of the airway.20

At the same time, afferent signal arising from the ISLN receptor field is essential for ensuring the effective closure of the larynx and preventing of aspiration. Silencing ISLN activity by anesthetic blockade causes a failure in the control of laryngeal closure.21 Therefore it is important to reduce laryngeal pressor and cardiovascular response without inducing airway obstruction or aspiration in topical anesthesia of upper airway tract. In the present study, only glottic-supraglottic regions were anesthetized under direct vision. We aimed for maximum blunting of laryngeal reflex by merely ISLN anesthesia and preserving laryngeal patency and closure function as much as possible. The mentioned area is not only rich with innervations that includes intense laryngeal reflexes, but also the area mainly exposed with surgical and intubation trauma.

Only 6 puffs (60 mg) of topical lidocaine were administered to all patients in our study. We aimed to use the minimum dose of lidocaine to minimize area (supraglottic and glottic region) to prevent the leakage of lidocaine and deep

Table 4. Mean values and SD of systolic-diastolic blood pressure in control group and in study group.

<table>
<thead>
<tr>
<th>Blood pressure</th>
<th>Control group</th>
<th>Study group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean value</td>
</tr>
<tr>
<td>BPBINDS</td>
<td>27</td>
<td>125.73</td>
</tr>
<tr>
<td>BPBINDD</td>
<td>27</td>
<td>81.59</td>
</tr>
<tr>
<td>BPAINDS</td>
<td>27</td>
<td>138.37</td>
</tr>
<tr>
<td>BPAINDD</td>
<td>27</td>
<td>86</td>
</tr>
<tr>
<td>BPBINITS</td>
<td>27</td>
<td>140.96</td>
</tr>
<tr>
<td>BPBINTD</td>
<td>27</td>
<td>92.22</td>
</tr>
<tr>
<td>BPAINTS</td>
<td>27</td>
<td>151.93</td>
</tr>
<tr>
<td>BPAINTD</td>
<td>27</td>
<td>96.37</td>
</tr>
<tr>
<td>BPBSURS</td>
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<td>144.44</td>
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<tr>
<td>BPBSURD</td>
<td>27</td>
<td>95.67</td>
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<tr>
<td>BPASURS</td>
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<td>134.48</td>
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<tr>
<td>BPASURD</td>
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<td>BPBEXTS</td>
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<td>BPAEXTS</td>
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<tr>
<td>BPAEXTD</td>
<td>27</td>
<td>90.22</td>
</tr>
</tbody>
</table>

Abbreviations: BPBINDS, blood pressure before induction-systolic; BPBINDD, blood pressure before induction-diastolic; BPAINDS, blood pressure after induction-systolic; BPAINDD, blood pressure after induction-diastolic; BPBINTS, blood pressure before intubation-systolic; BPBINTD, blood pressure before intubation-diastolic; BPAINTS, blood pressure after intubation-systolic; BPAINTD, blood pressure after intubation-diastolic; BPBSURS, blood pressure before surgery-systolic; BPBSURD, blood pressure before surgery-diastolic; BPASURS, blood pressure after surgery-systolic; BPASURD, blood pressure after surgery-diastolic; BPBEXTS, blood pressure before extubation-systolic; BPBEXTD, blood pressure before extubation-diastolic; BPAEXTS, blood pressure after extubation-systolic; BPAEXTD, blood pressure after extubation-diastolic.

Table 5. Incidence and severity of postoperative complications.

<table>
<thead>
<tr>
<th>Postoperative complications</th>
<th>Study group</th>
<th>Total</th>
<th>Control group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laryngospasm</td>
<td>2 (mild)</td>
<td>1</td>
<td>1 (mild)</td>
<td>1</td>
</tr>
<tr>
<td>Agitation</td>
<td>1 (mild)</td>
<td>1</td>
<td>3 (mild)</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>2 (moderate)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coughing</td>
<td>7 (mild)</td>
<td>9</td>
<td>7 (mild)</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>1 (moderate)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 (severe)</td>
<td></td>
<td></td>
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</tbody>
</table>
inhibition of the laryngeal reflexes, as high dose application of topical lidocaine can cause deep inhibition of laryngeal reflexes, which may cause aspiration. In the literature, the common application dose of topical lidocaine is over 120 mg, which is 2 times higher than our application dose.\textsuperscript{22,23} Toxicity of local anesthetics must be considered regardless the route of the administration. We did not measure plasma levels of lidocaine because 60 mg per patient is nowhere near the toxic dose of lidocaine (toxic dosage of lidocaine >300 mg).

Hemodynamic changes and respiratory complications generally increase due to painful stimulation and prolonged pressure by laryngoscopy blade.\textsuperscript{24,25} Pain and pressure applied during laryngeal microsurgery are noted to be higher in patients with difficult laryngeal exposure; however, they will differ individually. Intravenous methylprednisolone (2 mg/kg) was administrated to all patients to minimize individual response to pain and inflammation, for the purpose of preventing excessive responses due to difficult laryngeal exposure.

Kocamanoglu et al compared 4 groups: methylprednisolone 3 mg/kg, 0.9\% saline physiologic 5 ml, lidocaine 1.5 mg/kg intravenously, and 7 puffs of aerosolized 10\% lidocaine to oropharyngolaryngeal structures topically. They concluded that intravenous or topical administration of lidocaine was effective in reducing postoperative respiratory complications after short-term laryngeal surgery by way of rigid laryngoscope.\textsuperscript{26} Lee and Park, who investigated the hemodynamic changes and cough during extubation due to suspension laryngoscopy, showed mean arterial pressure (at 2.5 and 5 min after suspension laryngoscopy) and heart rate (at 2.5 min after suspension laryngoscopy) were greater in the control group than in the topical lidocaine administered group (1.5 mg/kg). In this study, 1.5 mg/kg of 10\% lidocaine was sprayed onto laryngeal and intratracheal sites 2 minutes prior to intubation. Also they noted that coughing was suppressed throughout the entire study.\textsuperscript{22} Our results show that 10\% lidocaine sprayed on supraglottic-glottic laryngeal site decreases systolic-diastolic blood pressures at pre- and post-extubation significantly. Heart rates and SPO\textsubscript{2} were not affected statistically. Laryngospasm and coughing were nearly the same in both groups, whereas agitation was significantly lower in study group.

We expected to see the effect of lidocaine during the surgery (laryngeal manipulation period) and extubation periods because topical lidocaine was applied at the post-intubation period. But there was no statistically difference observed in hemodynamics between study and control groups during the surgery period. The only significant difference in hemodynamics between 2 groups was systolic-diastolic blood pressure difference during the extubation period. We do not know the reason why the effect of lidocaine was seen during the extubation period but not seen during the surgery period. Lidocaine may be more effective for inhibiting superficial irritation during the extubation period than deep trauma caused by laryngoscope blade or surgical trauma.

Postoperative pain is one of the most important factors that cause agitation. Main causes of pain include surgical wounds, sore throat, and pressure of the blade.\textsuperscript{27} Topical lidocaine administration might reduce the pain and so the agitation in our study.

Blunting the sympathetic nervous system of the airway by lidocaine application was widely used before intubation and emphasized in the previous studies. However, larynx microsurgery has further cardiovascular response and can be fatal in patients who have hypertension, myocardial ischemia, or cerebrovascular disease. Topical lidocaine seems beneficial in attenuating cardiovascular responses to larynx microsurgery.

According to our results, 60 mg topically applied lidocaine attenuate stimuli due to suspension laryngoscopy; however, it is not effective for more serious respiratory complications such as laryngospasm and coughing. It was suggested that effective suppression of cough reflex required high lidocaine serum concentration, around 3 mg/ml, to attenuate the respiratory response.\textsuperscript{22,28,29} Sixty mg lidocaine may be a reason for decreased effectiveness regarding laryngospasm and coughing, but minimum dosage of lidocaine is mandatory because of increased aspiration risk and airway resistance. Hamilton et al indicate that desaturation was higher in patients receiving topical lidocaine when compared with patients who did not.\textsuperscript{30} We did not observe any SPO\textsubscript{2} change between the 2 groups, but mild laryngospasm that was relieved without treatment was seen in 1 more patient in the study group.

In the present study, topical 60 mg lidocaine administration before laryngeal microsurgery decreases blood pressure during extubation and relieves agitation during recovery. Higher dosage of lidocaine may diminish the incidence of laryngospasm and coughing with increased risk of aspiration and airway resistance.

**Conclusion**

Topical lidocaine administration before larynx microsurgery is effective in reducing blood pressure and agitation but not in abolishing the laryngeal and cardiovascular response totally. Further studies are required to determine the optimum dose of lidocaine for cardiovascular stability, airway security, and patient comfort during the postoperative period.

**Author Contributions**

Ilker Burak Arslan, substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; Isil Kose, substantial contributions to conception and design; Ejder Ciger, acquisition of data, or analysis and interpretation of data; Erhan Demirhan, acquisition of data, or analysis and interpretation of data; Murat Gumnussoy, acquisition of data, or analysis and interpretation of data; Ibrahim Cukurova, final approval of the version to be published.

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References


