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■ Clinical Research ■

The effect of combining lidocaine with dexamethasone for attenuating postoperative sore throat, cough, and hoarseness

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Background: Despite the established efficacy of dexamethasone and lidocaine for preventing postoperative airway symptoms, no study has investigated the effects of dexamethasone plus lidocaine for attenuating postoperative airway symptoms. The purpose of this study was to explore whether combined dexamethasone and lidocaine are superior to dexamethasone alone in reducing postoperative sore throat, cough, and hoarseness for 24 h after tracheal extubation.

Methods: In total, 70 female patients undergoing breast mass excision were randomized in a prospective, double-blinded manner into two groups: Group DL received intravenous dexamethasone (8 mg) plus lidocaine (1.5 mg/kg) 5 min before induction of anesthesia, and lidocaine was injected once more at the end of surgery. Group D received dexamethasone (8 mg) plus normal saline instead of lidocaine in the same manner as Group DL. We assessed the incidence and severity of postoperative sore throat, cough, and hoarseness 1 and 24 h after extubation.

Results: The incidence of sore throat for 24 h after tracheal extubation was significantly lower in Group DL than in Group D (62.9% vs. 85.7%, respectively; P = 0.029). The severity of sore throat and hoarseness for 24 h after extubation was lower in Group DL than in Group D ($P < 0.05$). The incidence and severity of cough did not differ between the two groups for 24 h after extubation.

Conclusions: Lidocaine combined with dexamethasone is more effectively reduces the incidence and severity of sore throat and severity of hoarseness for 24 h after extubation in patients who have undergone breast mass excision surgery. **(Anesth Pain Med 2016; 11: 42-48)**

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INTRODUCTION

Postoperative sore throat, post-extubation coughing, and hoarseness are common complications after general anesthesia using endotracheal tubes. The reported incidence varies from 30% to 81% [1-4]. These laryngopharyngeal complications contribute to postoperative morbidity and reduce patient satisfaction [5]. Various methods such as licorice gargle, inhaled fluticasone propionate, aspirin and benzydamine hydrochloride gargles, lidocaine spray, intracuff alkalinized lidocaine, magnesium lozenge, stellate ganglion blockade, dexamethasone, and lidocaine injection have been introduced to minimize the incidence and severity of these complications [4,6-12]. Despite their effectiveness in alleviating the postoperative airway symptoms, many of these methods have limited applications because of their limited availability, requirement for patient cooperation, and patient inconvenience [6]. However, administration of intravenous dexamethasone and lidocaine is simple, effective, easily available, and practicable in the operating room.

Prophylactic dexamethasone injection prior to anesthesia induction reduces the incidence and severity of postoperative sore throat and hoarseness [11,13]. In addition, intravenous lidocaine prior to intubation or at the end of surgery reduces the incidence of postoperative sore throat and cough [12,14]. As mentioned above, the efficacy of intravenous dexamethasone and lidocaine in minimizing the incidence and severity of postoperative airway symptoms is well-established. However, no study has compared the effects of dexamethasone plus lidocaine combination therapy with the effects of prophylactic dexamethasone alone. Considering the multifactorial etiology of postoperative sore throat [14,15], we hypothesized that combined dexamethasone and lidocaine would be more effective

than dexamethasone alone in reducing postoperative throat problems. Therefore, the incidence and severity of postoperative sore throat, cough, and hoarseness were evaluated among patients undergoing breast mass excision under general anesthesia using an endotracheal tube to evaluate whether combined dexamethasone and lidocaine are superior to dexamethasone alone in reducing postoperative laryngopharyngeal complications.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board of our hospital. Written informed consent was obtained from all trial participants. Female nonsmoking patients with an American Society of Anesthesiologists (ASA) physical status of I or II undergoing elective surgery for breast mass excision under general anesthesia were included. Patients were excluded if any of the following criteria were fulfilled: a history of preoperative sore throat, cough, and hoarseness; a history of upper respiratory infection within the last 2 weeks; allergy or hypersensitivity to local anesthetics; preoperative treatment with analgesics or corticosteroids; any contraindication to corticosteroid medications; and more than one attempt at orotracheal intubation. The study was conducted in a prospective, randomized, and double-blinded manner. Patient randomization was performed using the sealed envelope method, in which patients were randomly allocated in a ratio of 1 : 1 to receive one of the two assigned medications: patients in Group D received dexamethasone (8 mg) plus normal saline, and those in Group DL received dexamethasone (8 mg) plus lidocaine (1.5 mg/kg).

Upon the patient's arrival to the operating room, routine noninvasive pulse oximetry, electrocardiography, and noninvasive blood pressure monitoring were started before premedication. Five minutes prior to the induction of anesthesia, dexamethasone (8 mg) plus lidocaine (1.5 mg/kg) (Group DL) or dexamethasone (8 mg) plus an equal volume of normal saline (Group D) was injected intravenously. Anesthesia was induced with intravenous injection of thiopental (5 mg/kg) and fentanyl (1 μg/kg), and orotracheal intubation was facilitated with intravenous injection of vecuronium (0.1 mg/kg). An endotracheal tube with a 7-mm internal diameter (ID) and a high-volume/low-pressure cuff (Euromedical, Kedah, Malaysia) was used. The endotracheal tube was lubricated with normal saline. Laryngoscopy was performed by the same anesthesiologist in both groups using standard size 3 Macintosh metal blades. The cuff was inflated until no air leakage could be heard with the presence of positive airway pressure at 20 cmH_2O. Neither an oral airway nor bite block was used in any patient. After anesthetic induction, all patients received palonosetron (0.075 mg) to prevent postoperative nausea and vomiting. Anesthesia was maintained with N_2O : O_2 (1 : 1) and sevoflurane (1.0–2.5 vol% end-tidal concentration). Controlled mechanical ventilation with an initial tidal volume of 8 ml/kg and respiratory frequency of 12 breaths/min was adjusted to maintain normocapnia. To limit increases in the nitrous oxide-related intracuff pressure, the intracuff pressure was adjusted with a noninvasive manometer (Mallinckroft Medical, Athlone, Ireland) every 20 min and maintained at $<$ 20 cmH_2O during the operation. In both groups, no humidifiers or heat and moisture exchangers were used; instead, a general respiration circuit was used. Upon completion of surgery, the inhalational anesthetics were turned off and 1.5 mg/kg of lidocaine (Group DL) or an equivalent volume of normal saline (Group D) was administered intravenously. Residual neuromuscular block was antagonized with pyridostigmine (10 mg) and glycopyrrolate (0.2 mg), and the lungs were ventilated with 100% O_2 until the patient was fully awake and had recovered from the muscle relaxant. After confirming adequate spontaneous ventilation and response to verbal commands, tracheal extubation was immediately performed by the anesthesiologist after suctioning of the oropharynx. Prior to extubation, gentle oropharyngeal suctioning of oral secretions using a soft rubber catheter was performed to minimize injury to tissues in the oral cavity. After extubation, all patients were transferred to the post-anesthesia care unit. Intravenous tramadol (50 mg) was administered when patients required additional postoperative pain control.

Measurements

Demographic data, the time needed for intubation (time from opening the mouth to successful tracheal intubation), intubation period (time from intubation to extubation), grade of laryngoscopic view using the Cormack-Lehane score [16], incidence of bucking or coughing during tracheal intubation and extubation, application of external laryngeal pressure to facilitate endotracheal intubation, blood in the secretions or endotracheal tube, and recovery time (time from the end of the operation to extubation) were recorded by an anesthetic nurse who was blinded to the study.

Postoperative sore throat, cough, and hoarseness were evaluated using direct questions [17] at 1 and 24 h after tracheal extubation by an anesthesia resident who was blinded to the

study. The severity of postoperative sore throat and cough was graded on a 4-point scale (0–3): 0, no sore throat or cough; 1, mild sore throat or cough (less than a common cold); 2, moderate sore throat or cough (similar to a common cold); and 3, severe sore throat or cough (more than a common cold) [7]. The severity of postoperative hoarseness was also graded on a 4-point scale (0–3): 0, no hoarseness; 1, hoarseness at the time of interview, but noted only by the patient; 2, hoarseness that is readily apparent, but mild; and 3, hoarseness that is readily apparent and severe [2]. The primary outcome of this study was the incidence of sore throat for 24 h after surgery. The secondary outcome included the incidence of cough and hoarseness and the severity of sore throat, cough, or hoarseness for 24 h after surgery.

To exclude the masking effects of surgical pain and systemic analgesics, we also recorded the numerical rating scale scores (0 = no pain, 10 = worst pain imaginable) for surgical wound pain and total amount of tramadol administration for 24 h after the surgery.

Statistical analysis

Data were analyzed using SPSS software (ver. 18.0 for Windows; SPSS Inc., Chicago, IL, USA). The primary outcome variable was the incidence of sore throat for 24 h after surgery. Based on a previous study that showed a 69% incidence of sore throat for 24 h after surgery in the prophylactic dexamethasone (10 mg) group [2], we considered a 50% reduction of this incidence in Group DL as clinically significant. For a power of 0.8 and α-value of 0.05 (2-sided), a sample size of 32 for each group was required. Thus, considering a potential dropout rate of 10%, we enrolled 36 patients per group. Differences in continuous variables between the groups were compared using Student's *t*-test. Between-group differences in categorical variables were analyzed using the χ^2-test or Fisher's exact test, as appropriate. The severity scores of sore throat, cough, and hoarseness were compared using the Mann-Whitney *U* test. P values of < 0.05 were considered to indicate statistical significance.

RESULTS

Of the 75 patients enrolled in the study, 3 were excluded (2 declined to participate and 1 was a smoker). Additionally one patient each in Group D and DL was withdrawn because they required more than one intubation attempt. Thus, 70 patients were included in the final analysis (Fig. 1).

There were no significant differences in patient characteristics between the two groups (Table 1). Intraoperative

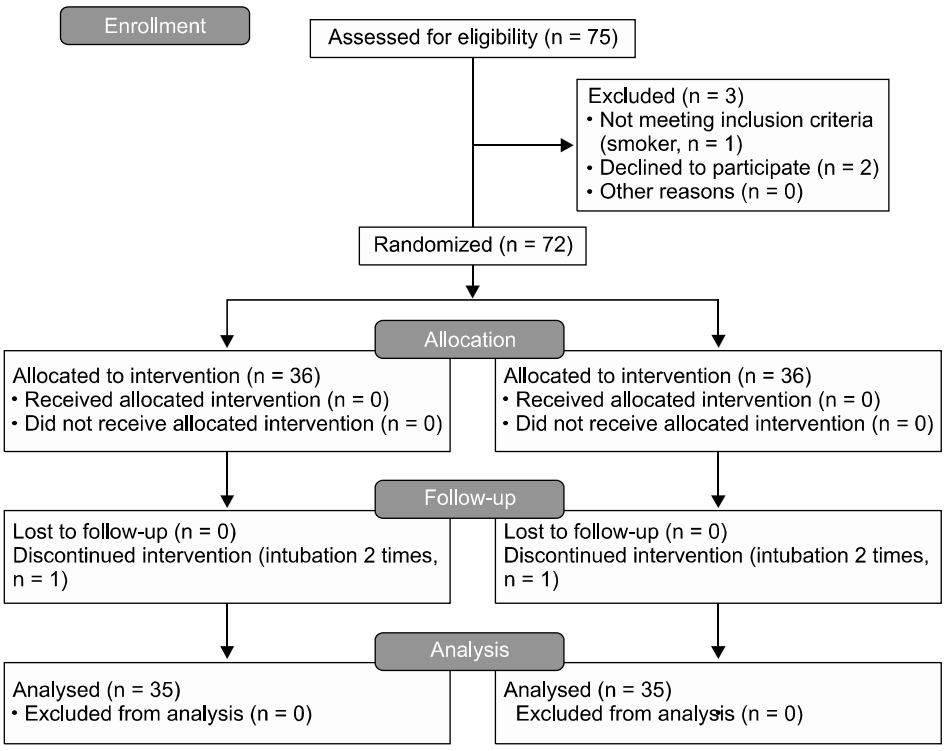

Fig. 1. Flow diagram of study enrollment and randomization.

variables are shown in Table 2; there were no significant differences in intubation time, application of external laryngeal pressure, the incidence of bucking or coughing during tracheal intubation and extubation, blood in the secretions or tracheal tube, or recovery time between the two groups.

Postoperative wound pain at 1 and 24 h after the operation was significantly greater in Group D than in Group DL (NRS score, 4.9 ± 2.0 and 1.9 ± 1.4 vs. 3.7 ± 1.7 and 1.3 ± 1.1, respectively; P = 0.009 and P = 0.039, respectively). The doses of tramadol required for 24 h after the operation were also significantly higher in Group D than in Group DL (20.0 ± 32.5 vs. 7.1 ± 17.8 mg, respectively; P = 0.045) (Table 2).

As the primary outcome, the incidence of sore throat for 24 h after the operation was significantly higher in Group D than in Group DL (30 [85.7%] vs. 22 [62.9%] patients, respectively; P = 0.029). The incidence of sore throat at 1 and 24 h after the operation was significantly higher in Group D than in Group DL (28 [80%] and 18 [61.4%] vs. 20 [57.1%] and 8 [22.9%], respectively; P = 0.039 and P = 0.013, respectively) (Fig. 2). As a secondary outcome, the incidence of cough and hoarseness for 24 h after surgery were equal and similar, respectively, in Groups D and DL (17 [48.6%] vs. 17 [48.6%] for cough and 28 [80.0%] vs. 24 [68.6%], respectively; P = 0.274 for hoarseness) (Table 2). However, the incidence of hoarseness at 24 h after extubation was significantly higher in Group D than in Group DL (16 [45.7%] vs. 6 [17.1%], respectively; P = 0.010) (Fig. 2).

The severity scores for sore throat and hoarseness at 1 and

Table 1. Patient Characteristics

	Group D (n = 35)	Group DL (n = 35)	P value
Age (yr)	42.3 ± 9.3	44.8 ± 7.6	0.231
Height (cm)	159.5 ± 4.8	157.3 ± 5.6	0.081
Weight (kg)	57.1 ± 9.1	57.9 ± 8.7	0.697
ASA physical status (I/II)	29/6	25/10	0.255
Cormack-Lehane grade (I/II/III/IV)	19/10/6/0	18/13/4/0	0.870
Local excision of breast mass			
Unilateral/bilateral	30/5	28/7	0.526
Duration of surgery (min)	36.3 ± 16.1	33.3 ± 13.8	0.414
Duration of intubation (min)	56.0 ± 16.7	53.6 ± 13.2	0.502

Data presented as mean ± standard deviation or number of patients. Group D: Dexamethasone group, Group DL: Dexamethasone pluslidocaine group, ASA: American Society of Anesthesiologists.

Table 2. Intraoperative Variables and Clinical Outcomes

	Group D (n = 35)	Group DL (n = 35)	P value
Time taken to intubate (s)	21.9 ± 9.2	18.8 ± 5.4	0.090
External laryngeal pressure	10 (28.6)	11 (31.4)	0.794
Bucking or coughing during intubation	3 (8.6)	4 (11.4)	1.000
Bucking or coughing during extubation	9 (25.7)	10 (28.6)	0.788
Blood in the secretions or tube	8 (22.9)	5 (14.3)	0.540
Recovery time (min)	7.9 ± 2.1	8.5 ± 2.2	0.289
Wound pain NRS score (0–10)			
1 h	4.9 ± 2.0	3.7 ± 1.7	0.009
24 h	1.9 ± 1.4	1.3 ± 1.1	0.039
Dose of tramadol administered (mg)	20.0 ± 32.5	7.1 ± 17.8	0.045
During the 24 h after the surgery			
Sore throat	30 (85.7)	22 (62.9)	0.029
Cough	17 (48.6)	17 (48.6)	1.000
Hoarseness	28 (80.0)	24 (68.6)	0.274

Data presented as mean ± SD or number of patients (%). Group D: Dexamethasone group, Group DL: Dexamethasone plus lidocaine group, NRS: numerical rating scale.

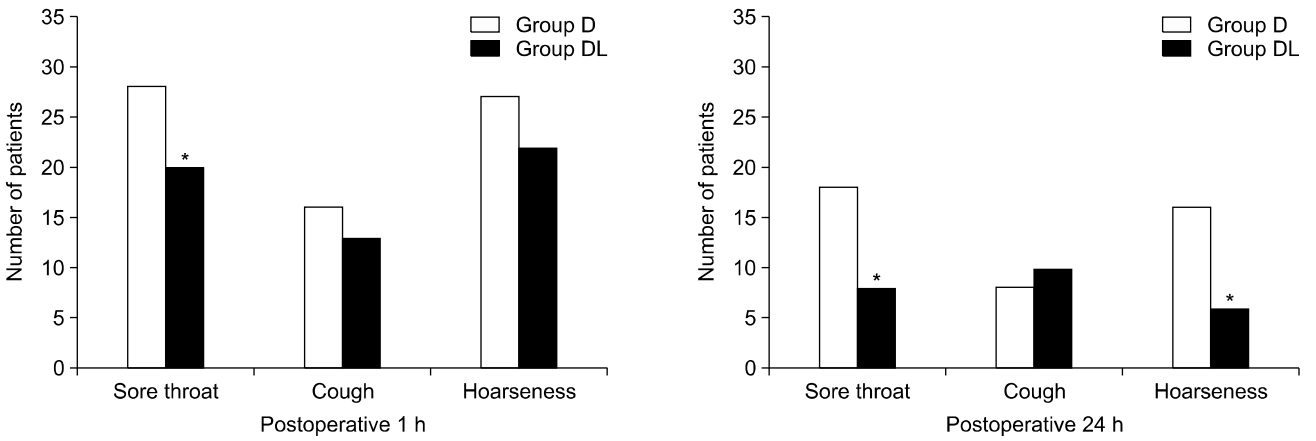

Fig. 2. Incidence of postoperative sore throat, cough, and hoarseness at 1 and 24 h after extubation. Data shown represent numbers of patients. *P < 0.05 between Groups D and DL.

Table 3. Severity Scores for Postoperative Sore Throat, Cough, and Hoarseness

	Group D (n = 35)				Group DL (n = 35)				P value
Severity score	0	1	2	3	0	1	2	3	
Sore throat									
1 h	7	11	11	6	15	12	7	1	0.009
24 h	17	12	5	1	27	7	1	0	0.009
Cough									
1 h	19	11	3	2	22	11	1	1	0.359
24 h	27	7	1	0	25	8	2	0	0.558
Hoarseness									
1 h	8	7	17	3	13	16	6	0	0.004
24 h	19	11	3	2	29	6	0	0	0.006

Data are presented as number of patients. Group D: Dexamethasone group, Group DL: Dexamethasone plus lidocaine group.

24 h after surgery were significantly higher in Group D than in Group DL (P = 0.009 and 0.009, respectively, for sore throat; P = 0.004 and 0.006, respectively, for hoarseness) (Table 3). The severity score of cough at 1 h and 24 h after the surgery was not significantly different between the two groups (Table 3).

DISCUSSION

The present study demonstrated that lidocaine combined with dexamethasone reduced the incidence and severity of postoperative sore throat compared with dexamethasone alone in female patients undergoing breast mass excision. The combination of dexamethasone and lidocaine also reduced the severity of hoarseness for 24 h after endotracheal extubation, and the incidence of hoarseness was measured at 24 h after extubation, although the incidence and severity of cough did not differ between the groups.

The main cause of postoperative sore throat is considered to be irritation and inflammation of the tracheal and pharyngolaryngeal mucosa [18], and the contributing factors are known to be age, sex, type of procedure, surgical manipulation of the airway, size and cuff pressure of the endotracheal tube, use of succinylcholine, use of a nasogastric tube, and excessive oral suctioning [19,20].

In the present study, to avoid potential confounding factors that may affect the incidence and severity of postoperative sore throat, cough, and hoarseness, we selected breast mass excision surgery that could be performed in identical-sex patients with similar ages (mainly middle-aged women), used the same size of endotracheal tube between the two groups, minimized surgical excision, decreased the requirement of postoperative analgesics, and used a surgical site distal to the airway structures.

In previous studies [4,9,21], an intravenous dexamethasone dose of > 0.1 mg/kg reduced the incidence and severity of postoperative sore throat on the first postoperative day. Intravenous lidocaine (1–2 mg/kg) also decreased the risk and severity of postoperative airway symptoms resulting from intubation [3,12,14].

Dexamethasone is a potent synthetic glucocorticoid with anti-inflammatory, antiemetic, and analgesic effects [22]. The mechanism of dexamethasone for reducing post-intubation airway complaints is mainly associated with its anti-inflammatory effects; dexamethasone may modulate the capacity of the endothelium to respond to inflammatory stimuli by preventing the recruitment of leukocytes and neutrophils, inhibiting the release of cytokines, and promoting the formation of prostaglandins and leukotrienes [23].

Lidocaine, the first aminoamide local anesthetic, has been commonly used to suppress airway reflexes, reduce bronchial hyper-reactivity, and attenuate hemodynamic responses from intubation due to its analgesic and anti-inflammatory properties [24]. Although the exact mechanism of lidocaine for suppressing postoperative airway symptoms remain unclear, it is possible that lidocaine suppresses the excitation of airway sensory C fibers and the release of sensory neuropeptides [25].

In the present study, contrary to sore throat and hoarseness, lidocaine combined with dexamethasone did not affect the incidence of postoperative cough compared with dexamethasone alone. Although the reason is unclear, we suspect that the dose of lidocaine in the current study may have been insufficient to additionally suppress a cough that has already been suppressed by intravenous dexamethasone [26]. Intravenous lidocaine decreased the incidence of coughing in a dose-dependent manner, and 2 mg/kg of lidocaine did not show significant suppressive effects on the cough reflex at 5 min after injection [24]. Another presumption is that sore throat and hoarseness may be more strongly influenced by the postoperative analgesic effect of lidocaine than cough. Thus, postoperative sore throat is associated with postoperative analgesia [27].

Intravenous dexamethasone and lidocaine administration during surgery significantly decrease the postoperative pain intensity [28,29]. Interestingly, lidocaine combined with dexamethasone more strongly reduced the postoperative wound pain and analgesic requirement for postoperative pain control than did dexamethasone alone in the present study. Painful surgical wounds and a high dose of postoperative systemic analgesics can mask postoperative airway symptoms. In the present study, however, despite the relatively lower surgical wound pain score and lower use of systemic analgesics (tramadol), lidocaine combined with dexamethasone reduced the incidence and severity of sore throat compared with dexamethasone alone.

The incidence of sore throat and hoarseness in the present study was higher than predicted [11,12,14]. This may be explained as follows. First, the incidence of sore throat, cough, and hoarseness was evaluated using a direct questioning method in this study. Direct questioning significantly increased the incidence of postoperative sore throat in a previous study [17]. Second, all patients were female, had an ASA status of I or II, and had a mean age of 42 (Group D) and 45 (Group DL) years. Furthermore, an endotracheal tube with a 7.0 mm ID and nitrous oxide gas were used for general anesthesia in this study. Female sex, the use of endotracheal tube with a 7.0 mm ID compared with 6.0 mm, an ASA status of I to II compared with III, and an age of > 40 years are associated with an increased risk of postoperative sore throat [15,20].

Potential serious side effects of dexamethasone or adverse effects of lidocaine injection for preventing sore throat have not been reported [3,21]. Some studies have suggested that intravenous lidocaine at the end of surgery may be associated with prolonged recovery [14], but in this study, the recovery time did not differ between the two groups despite the administration of lidocaine both before anesthesia induction and at the end of surgery.

This study has several limitations. First, we did not include a lidocaine alone group. Therefore, it remains unclear whether the combination of dexamethasone and lidocaine is superior to lidocaine alone in reducing postoperative airway symptoms. Second, we performed intravenous injections of lidocaine both before anesthesia induction and at the end of surgery. Thus, we could not determine the most effective timing and dose of lidocaine in combination with dexamethasone for preventing postoperative sore throat, cough, and hoarseness.

In conclusion, intravenous lidocaine given 5 min before anesthesia induction and at the end of surgery combined with prophylactic dexamethasone is more effective in reducing the incidence and severity of postoperative sore throat and the severity of hoarseness than prophylactic dexamethasone alone for 24 h after tracheal extubation in patients undergoing local breast mass excision.

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