Comparing the Suppressing Effect of Dexmedetomidine versus Lidocaine in Cough during Anesthesia Emergence: A Double-Blinded Randomized Clinical Trial

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ABSTRACT

Background: Cough, laryngospasm, bronchospasm, and tachycardia are physiological responses during anesthesia emergence (AE) and endotracheal extubation. The study addressed the efficacy of dexmedetomidine (DEX) versus lidocaine (LID) in suppressing cough during AE. Materials and Methods: A double-blinded randomized clinical trial enrolled 120 eligible hospitalized patients undergoing general anesthesia. Patients randomly assigned into three groups who (1) infused 0.5 mcg/kg intravenous (IV) DEX, (2) 1.5 mg/kg IV LID, and (3) 10 mL of normal saline (PBO), 10 min before anesthesia. The laryngospasm, cough frequency (CF) and duration of surgery among the groups (P > 0.05), but DEX having lower HR and CF (P < 0.05). A significant statistical difference was observed in RS except at 50 and 60 min (P < 0.05), with a lower RS in the LID and DEX than in the PBO, but both intervention groups were not different. Conclusion: Although RS in the DEX is not different from the LID, DEX demonstrates a reduced HR and CF and appears to be an appropriate drug without side effects on suppressing cough during AE.

Key words: Cough suppression during anesthesia emergence, dexmedetomidine, lidocaine

INTRODUCTION

Physiological responses remain common during anesthesia emergence (AE) and endotracheal (ET) extubation, causing complications including cough, laryngospasm, bronchospasm, and tachycardia.[1,2] The frequently cited complaints following anesthesia include postoperative airway complications such as sore throat, cough, and sputum, among which postextubation cough has been repeatedly reported to be associated to mechanical irritations such as external pressure, the ET intubation method, ET cuff, ET tube (ETT) size, and so forth,[3] and is though, usually not believed to be a serious complication from anesthesia, it is undesirable and sometimes occurs as an attack, increasing intracranial, intraocular and intra-abdominal pressures.[4,5] Intravenous (IV) lidocaine (LID) affected and reduced the intensity of postintubation cough owing to various causes, such as the laryngoscope blade type, straining during ET extubation, and smoking. After the intubation, cuff inflation will pack around the ETT and irritate the trachea.[4] This causes coughing when the depth of general anesthesia is low and causes many problems. ET and cuff irritation causes the complication and is the underlying mechanism. High-speed receptors in the tube are abundant and appear to play a key role in coughing.[6,7] These irritations are blocked during general anesthesia.[5,6]

Cough during emergence from general anesthesia increases blood pressure (BP), heart rate (HR) and myocardial ischemia, bronchospasm, and bleeding.[8] multiplies the pain caused by surgery, and increases intracranial and intraocular pressure in patients with brain involvement or glaucoma.[9,10] A range of methods is available, such as local and IV injection of topical anesthetics to reduce cough.[5,6,11] Furthermore, IV use of opioids is an alternative to reducing
cough at the end of the operation and during ET extubation, and when the patient does not complete awakening. However, this has frequently not been desirable. The use of topical anesthetics before ET intubation covers a limited time during surgery owing to absorption from the ETT mucus, and subsequently, a further alternative should be employed to achieve a more long-time effect. The intracuff method appears to arrive at the goal. LID reduces goblet cell secretion by controlling the neural pathway, although water absorption is besides reduced by LID effect on ion transport. The use of LID appears to influence the consequences in different ways.

Dexmedetomidine (DEX) is an α2-adrenoceptor agonist with antinociceptive, sedative, and hypotensive actions, and if infused, it reduces HR, systemic vascular resistance, and BP. This, as an adjuvant to induce general anesthesia with a central sympathetic effect, helps to maintain the patient’s hemodynamic status, and has a potent anesthetic effect reducing the need for opioids, complications, and stress response, as well as improving recovery. The DEX’s ability to provide adequate sedation and amnesia seems to remain matchless and causes a mild cognitive impairment that facilitates easy communication between the medical team and the patient in the intensive care unit and those in need of monitoring.

Different studies found a lower HR and mean BP (MBP) in patients receiving DEX, suggesting that the drug be used to reduce the amount of bleeding. As reported by Lee et al., DEX alone reduced cough more effectively than remifentanil alone, while no decrease in respiratory rate was observed in patients. Furthermore, other studies suggested that DEX and LID, respectively, reduces cough. Given that the effects of both DEX and LID have been so far studied alone, but not compared, hence, this led us to decide to conduct a study to address the compared efficacy of DEX and LID on reducing cough severity.

MATERIALS AND METHODS

The double-blinded trial enrolled 102 patients undergoing general anesthesia who hospitalized at Valiasr Hospital (Arak, Iran), after obtaining written consent and verification of inclusion/exclusion criteria. Inclusion criteria were patients who were 20–60 years of age, American Society of Anaesthesiologists I–II, Mallampati Class I–II, both genders, nonaddiction, nonsmoking, no active airway infection or history of surgery and pathology of larynx and trachea, absence of lower esophageal sphincter incompetence (absence of reflux), absence of body mass index >30, lack of intracranial and intraocular pressure, surgery time ranged between 60 and 120 min, no pulmonary and heart disease, and no use of drugs causing cough. Exclusion criteria were including lack of patient’s cooperation and satisfaction and death.

Sample size calculation was estimated by considering study power = 80% and type one error = 0.05. The written informed consent was obtained from all the participants and the study protocol approved by Ethical Committee of Arak University of Medical Sciences by code IR.ARAKMU.REC.1397.140. Moreover, the protocol registered at the Iranian Registry Clinical trial center by code IRCT20141209020258N97.

Eligible participants were assigned into three groups including DEX, LID, and normal saline (PBO) by block random allocation method.

All patients were hospitalized at least 1 day before surgery, kept NPO for 8 h, and afterward randomly split into three groups. All patients underwent the same anesthesia protocol, receiving 5 mL/kg IV crystalloid Ringer’s solution before induction of anesthesia, followed by 1 μg/kg fentanyl and 2 mg IV midazolam, and subsequently, anesthesia unconsciousness was induced with 5 mg/kg thipental sodium and 0.5 mg/kg IV atracurium after preoxygenation. This was followed by a direct laryngoscopy via Macintosh blade and ET intubation by PVC-cuffed ET (Flexicare Medical Ltd, UK) with appropriate size for each patient. We inflated the cuff with a cuff gauge providing a pressure of 25 cmH₂O to keep ETT cuff pressure the same for all patients. Thus, all participants were in the same condition for irritation of the ETT cuff. Anesthesia was continued through 75–150 μg/kg propofol infusion per minute and repeated muscle relaxant and opioid.

Participants were randomly split into three groups around 10 min before surgery: the DEX, LID, and PBO, being slowly infused 0.5 mcg/kg IV DEX, 1.5 mg/kg LID, and normal saline, respectively, in a 10-mL volume (for each) over 10 min. At the end of the operation, the ETT was removed after clearing any secretions from the upper airway when following adequate spontaneous respiration and complete awakening of the patient (obeying verbal commands such as opening the eyes, raising the head for 5 s). Subsequently, we assessed and recorded laryngospasm and cough at 0 and 10 min, and during recovery up to 40 min after ET extubation, whereas one did their prevalence in all patients. A cough is considered real when the patient spontaneously and quickly exhales, whereas the sound of a cough is heard. SaO₂ by pulse oximetry was evaluated and recorded all the time before induction of anesthesia and throughout surgery and during ET extubation at 0, 5 min,
and every 5 min up to 40 min after extubation, recovery time, and finally when transferring to the ward.

We assessed and recorded the changes in MAP by a noninvasive BP monitor attached to the patient and HR changes by electrocardiogram throughout the surgery, as well as 5–40 min after ET extubation. Ramsay score (RS) was assessed at the time of recovery and 10, 20, 30, 40, 50, and 60 min postoperatively. It should be noted that data were measured and recorded to conduct a double-blind study by an intern, without any awareness of the patient groupings, when for each group, preparation and administration of adjuvants were done by an anesthesiologist, whereas the patients were not aware of the group they were in. Data were analyzed using descriptive statistics, analysis of variance (ANOVA), Chi-square, and ANOVA for repeated-measures tests by SPSS software version 20.

RESULTS

A randomized, double-blind randomized clinical trial conducted on 102 eligible patients undergoing general anesthesia who were randomly assigned into three groups, including DEX, LID, and PBO. The mean age of patients in the study was 38.08 ± 7.49 years and the minimum and maximum ages was 19 and 50 years, respectively. As table 1, sex distribution showed that 74 (51.39%) were males and 70 (48.61%) female. Based on the results, no significant difference was seen in age (P = 0.876) and gender (P = 0.753), as well as changes in SaO₂ among the four groups (P < 0.05).

According to Figure 1, no statistically significant difference was found in MBP among the three groups at different time after extubation (P > 0.05). However, based on repeated-measure test, there was a significant difference in trend of MBP during study among three groups and the MBP was higher in DEX group (P = 0.038). Moreover, as showed in Figure 2, no statistically significant difference was found in mean of SaO₂ among the groups at different time after extubation (P < 0.05) except at 5th min (P = 0.23). Repeated-measure test did not show significant difference in trend of SaO₂ during study among three groups (P = 0.468).

Based on the results in Table 2, a significant difference was seen in HR among the groups at different times after extubation (P < 0.05). Based on repeated-measure test, lower HR observed in the DEX and LID than the PBO,

| Variable                  | Group | P   |
|---------------------------|-------|-----|
| Age, mean±SD              | DEX   | 38.17±7.60 | 0.900 |
|                          | LID   | 37.61±7.33 |
|                          | PBO   | 38.44±7.71 |
| Duration of surgery, mean±SD | DEX   | 91.85±9.90  | 0.899 |
|                          | LID   | 92.20±11.56 |
|                          | PBO   | 91.11±7.87  |
| Gender, n (%)             | Female | 17 (50)    | 0.941 |
|                          |      | 17 (50)   |
|                          | Male  | 16 (47)    | 14 (53) |
|                          |      | 17 (50)    |

Table 1: Comparison of mean±standard deviation of age, surgery duration, and sex distribution in dexmedetomidine, lidocaine, and normal saline groups

| HR at postextubation     | Group, mean±SD | P   |
|--------------------------|----------------|-----|
| Immediately              | DEX           | 80.97±8.52 | <0.001 |
|                          | LID           | 81.29±8.27 |
|                          | PBO           | 81.35±8.28 |
| 5th min                  | DEX           | 81.29±8.27 | <0.001 |
|                          | LID           | 81.32±8.30 |
|                          | PBO           | 81.35±8.28 |
| 10th min                 | DEX           | 82.29±7.66 | <0.001 |
|                          | LID           | 82.32±7.83 |
|                          | PBO           | 82.61±7.99 |
| 15th min                 | DEX           | 82.32±7.83 | <0.001 |
|                          | LID           | 82.61±7.99 |
|                          | PBO           | 82.32±7.83 |
| 20th min                 | DEX           | 83.38±7.22 | <0.001 |
|                          | LID           | 82.76±8.01 |
|                          | PBO           | 82.76±8.01 |
| 25th min                 | DEX           | 83.38±7.22 | <0.001 |
|                          | LID           | 82.76±8.01 |
|                          | PBO           | 82.76±8.01 |
| 30th min                 | DEX           | 83.38±7.22 | <0.001 |
|                          | LID           | 82.76±8.01 |
|                          | PBO           | 82.76±8.01 |
| 35th min                 | DEX           | 83.38±7.22 | <0.001 |
|                          | LID           | 82.76±8.01 |
|                          | PBO           | 82.76±8.01 |
| 40th min                 | DEX           | 83.38±7.22 | 0.002  |
|                          | LID           | 82.76±8.01 |
|                          | PBO           | 82.76±8.01 |

Table 2: Comparison of mean and standard deviation of heart rate in three studied groups including in dexmedetomidine, lidocaine, and normal saline

SD: Standard deviation, DEX: Dexmedetomidine, LID: Lidocaine, PBO: Normal saline

Figure 1: Comparison of mean and trend of blood pressure in three studied groups including in dexmedetomidine, lidocaine, and PBO

Figure 2: Comparison of mean and trend of SaO₂ in three studied groups including in dexmedetomidine, lidocaine, and PBO
and based on the Tukey post hoc test, the HR was lower in DEX than LID group ($P = 0.001$).

The results showed in Table 3 revealed that a statistically significant difference was observed in mean of cough frequency (CF) among three groups at all times after extubation ($P < 0.05$), except at 35–40 min ($P = 0.072$). Based on the post hoc test, lower CF was observed in DEX group and was lower than PBO group. Moreover, Dex group had lower CF than the LID up to 20–25 min ($P < 0.05$).

Given the results in Table 4, a statistically significant difference was seen in RS among the groups except at 50th and 60th min after extubation ($P < 0.05$). However, in other times, RS was lower in the LID and DEX than in the PBO but did not observe any difference between two intervention groups.

Comparing laryngospasm among three groups showed that, no significant difference was observed among groups at different time after extubation ($P > 0.05$).

### DISCUSSION

A randomized, double-blind randomized clinical trial conducted on 102 patients undergoing general anesthesia in three assigned groups which no statistically significant difference was observed among them regarding to age, gender, BP, $\text{SaO}_2$, frequency of laryngospasm, and duration of surgery. Based on our results, HR and CF were lower in the DEX than the others. The DEX group had a lower HR and lower CF for 20–25 min, compared to the LID, but a significant statistical difference was seen in RS among the groups at the 50 and 60 min and RS was lower in LID and DEX than in the PBO. However, LID and DEX groups were same regarding to RS. Overall, the DEX caused reduction in HR and CF, compared to the LID and PBO, but RS in the group was not different from that in the LID.

DEX is an adjuvant to induce general anesthesia with a central sympathetic effect has a potent anesthetic effect reducing the need for opioids, complications, and stress response, as well as improving recovery.$^{[2,7,11,15]}$ DEX is an $\alpha_2$-adrenoceptor agonist with antinociceptive, sedative, and hypotensive actions and helps to maintain the patient’s hemodynamic status.$^{[2,16,17]}$ As this study showed, the DEX was more effective than LID in suppressing cough in patients undergoing anesthesia.

Hanci et al. study assessed the effects of fentanyl or DEX when used in combination with propofol and LID for tracheal intubation and showed that ET intubation was better with the DEX–LID–propofol combination than with the fentanyl–LID–propofol combination,$^{[18]}$ whereas our results showed that DEX reduces HR and CF, while RS in the DEX was not different from that in the LID.

Lee et al. conducted a study aimed at assessing the efficacy of single dose of DEX to reduce cough during anesthesia in which the DEX group had a lower frequency of cough and mean cough grade during ET extubation, while MBP and HR did not significantly differ. DEX though decreased cough effectively, compared with remifentanil, no decrease was found in respiratory rate in their patients.$^{[15]}$ Their results were in line with ours.

A systematic review showed that IV LID injection from 0.5 to 2 mg/kg, dose-dependently prevents intubation-, extubation-, and opioid-induced cough in adults and children with number needed to treat ranging from 8 to 3.$^{[6]}$ Nevertheless, our results suggested that LID as well as DEX was more effective than LID in suppressing cough in patients undergoing anesthesia.

### Table 3: Comparison of mean and standard deviation of (cough) cough frequency in three groups in three studied groups including in dexmedetomidine, lidocaine, and normal saline

| CF Group, mean±SD | P |
|-------------------|---|
|                   | DEX | LID | PBO |
| Immediately after extubation | 0.058±0.238 | 0.235±0.430 | 2.56±1.88 | <0.001 |
| Baseline | 0.058±0.238 | 0.235±0.430 | 2.94±1.29 | 0.008 |
| 5-10 min | 0.058±0.238 | 0.235±0.430 | 2.86±1.41 | 0.002 |
| 10-15 min | 0.058±0.238 | 0.235±0.430 | 2.31±1.32 | <0.001 |
| 15-20 min | 0.058±0.238 | 0.235±0.430 | 2.10±0.91 | 0.015 |
| 20-25 min | 0.058±0.238 | 0.235±0.430 | 1.69±0.55 | 0.012 |
| 25-30 min | 0.02±0.070 | 0.125±0.078 | 1.56±0.50 | 0.034 |
| 30-35 min | 0.012±0.070 | 0.086±0.016 | 1.12±0.35 | 0.039 |
| 35-40 min | 0.00±0.000 | 0.01±0.007 | 0.626±0.17 | 0.072 |

SD: Standard deviation, DEX: Dexmedetomidine, LID: Lidocaine, PBO: Normal saline, CF: Cough frequency

### Table 4: Comparison of mean and standard deviation of Ramsay score in three studied groups including in dexmedetomidine, lidocaine, and normal saline

| RS Group, mean±SD | P |
|-------------------|---|
|                   | DEX | LID | PBO |
| On arrival to recovery room | 2.23±0.553 | 2.08±0.287 | 1.88±0.327 | 0.002 |
| 10 min | 2.20±0.478 | 2.08±0.287 | 1.88±0.327 | 0.002 |
| 20 min | 2.17±0.386 | 2.08±0.287 | 1.89±0.287 | 0.004 |
| 30 min | 2.14±0.359 | 2.05±0.238 | 1.94±0.238 | 0.014 |
| 40 min | 2.11±0.327 | 2.02±0.171 | 1.94±0.238 | 0.019 |
| 50 min | 2.02±0.171 | 2.00±0.000 | 2.00±0.00 | 0.372 |
| 60 min | 2.00±0.11 | 2.00±0.00 | 2.00±0.00 | 1 |

SD: Standard deviation, DEX: Dexmedetomidine, LID: Lidocaine, PBO: Normal saline, RS: Ramsay score
significantly lower in the DEX, while nausea and vomiting were similar, and that DEX reduced cough and agitation in patients,[19] whose results were consistent with ours.

CONCLUSION
DEX decreased HR and CF in the LID and PBO, whereas RS in the DEX did not differ from that in the LID. DEX, like LID, seems to be a promising drug to suppress cough during AE, given the lack of side effects, and to be used as an option and drug choice to achieve the goal.

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Conflicts of interest
There are no conflicts of interest.

Disclosure
This material has never been published and is not currently under evaluation in any other peer reviewed publication.

Ethical approval
The permission was taken from Institutional Ethics Committee prior to starting the project. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent
Informed consent was obtained from all individual participants included in the study.

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