TEHRAN UNIVERSITY OF MEDICAL SCIENCES

Archives of Anesthesiology and Critical Care (In Press); x(x): xx-xx.

Available online at http://aacc.tums.ac.ir

Department of Anesthesiology, Pain and Critical Care Medicine TUMS

Research Article

Comparison of Transtracheal Dexmedetomidine with Transtracheal Lidocaine in Patients Undergoing Bronchoalveolar Lavage

Moein Daneshmand[1], Alireza Jahangirifard[2], Ali Nazembokaee[3], Marzie Shahrabi[4], Lida Fadaizadeh[5], Alireza Salimi[1], Kobra Rafiei[6]*

[1]Chronic Respiratory Diseases Research Center (CRDRC), National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[2]Lung Transplant Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[3]Anesthesiology and Critical Care Department University, Critical Care Quality Improvement Research Center, Masih Daneshvari Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[4]Department of Anesthesiology and Critical Care, School of Medicine, Shahid Modarres Hospital, Shahid Beheshti University of Medical Science, Tehran, Iran.

[5]Telemedicine Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran.

[6]Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

ARTICLE INFO

Article history:
Received 19 March 2025
Revised 09 April 2025
Accepted 23 April 2025

Keywords:
Transtracheal;
Dexmedetomidine;
Lidocaine;
Bronchoalveolar lavage

ABSTRACT

Background: Airway management is a routine part of any type of anesthesia; therefore, the present study was designed to compare the effect of transtracheal dexmedetomidine and transtracheal lidocaine in patients undergoing bronchoalveolar lavage and other adverse events.
Methods: Individuals aged 18 to 65 years that were candidates for bronchoalveolar lavage in three groups were included in the study. All three groups of patients underwent a standard treatment with the same anesthesia method with the same treatment group. Patients were administered lidocaine (4 cc 2% lidocaine), dexmedetomidine (0.5 g/kgµ dexmedetomidine), and lidocaine + dexmedetomidine (4 cc 2% lidocaine + 0.5 g/kgµ dexmedetomidine) groups.
Results: A total 150 patients with a mean age of 57.2±16.32 were evaluated in three equal groups. The clinical status of the patients showed that the patients in the combined use of dexmedetomidine and lidocaine group underwent sedation significantly more than the other two groups. The incidence of cough in dexmedetomidine and lidocaine group of patients was significantly lower than in the other groups.
Conclusion: The simultaneous use of transtracheal lidocaine and dexmedetomidine significantly reduces the incidence of cough in patients undergoing bronchoalveolar lavage.

The authors declare no conflicts of interest.
*Corresponding author.
E-mail address: abrisham57@gmail.com
DOI:

Introduction

Airway management is a routine part of general anesthesia and is associated with airway and hemodynamic responses like hypertension, tachycardia, dysrhythmias, myocardial ischemia, coughing, bronchospasm, postoperative bleeding, and raised intracranial pressure [1-4]. Studies have been carried out to assess the efficacy of various drugs in suppressing tracheal extubation responses [5-7]. Dexmedetomidine is a potent, highly selective alpha-2 adrenoceptor agonist that effectively reduces the airway and circulatory response during emergence from general anesthesia [8-12]. This medicine plays a significant role in reducing the pain and cough response caused by tracheal extubation by reducing the activity of the sympathetic nervous system and inducing relaxation. In addition to dexmedetomidine, lidocaine is known to be an effective anesthetic in suppressing the cough response after awakening from anesthesia. Lidocaine can be used as an aerosol, intratracheal, intravenous (IV) injection, and endotracheal cuff inflation to relieve responses after tracheal extubation. Sun et al. [9] conducted a meta-analysis to evaluate the efficacy and safety of intravenous lidocaine for suppression of the cough response after opioid administration. They found that the minimum optimal dose was 0.5 mg/kg. In addition, another meta-analysis confirmed the role of intravenous lidocaine in suppressing the cough response induced by opioid administration and cough after tracheal extubation in different age groups [6].

Recently, Fan et al. [10] compared the sedative effects of intravenous remifentanil and dexmedetomidine in a study and found that these drugs did not have a different sedative effect on cough severity after extubation. Despite the sedative effect and reduced post-recovery response of lidocaine and dexmedetomidine [13-24], the difference in efficacy of these drugs in reducing cough after recovery from anesthesia has not yet been confirmed.

We hypothesized that transtracheal dexmedetomidine could have similar positive effects as its infusion conditions. Therefore, the present study was designed to compare the effect of transtracheal dexmedetomidine and transtracheal lidocaine in patients undergoing bronchoalveolar lavage and other adverse events.

Methods

Patient collection and ethical considerations

The present study was conducted as a randomized clinical trial (RCT CODE) with the approval of the Ethics Committee in Biomedical Research of Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1403.078) at Masih Daneshvari Hospital.

A total of 66 patients who underwent bronchoalveolar lavage were randomly divided into three groups: dexmedetomidine, lidocaine, and dexmedetomidine + lidocaine (Figure 1).

For this purpose, individuals aged 18 to 65 years and of both sexes who were candidates for bronchoalveolar lavage at Masih Daneshvari Hospital, Shahid Beheshti University of Medical Sciences, Tehran, were included in the study. After evaluating the available records and documents and taking a history and examination at the preoperative anesthesia visit, individuals who met the exclusion criteria (history of allergy to anesthetic drugs, history of drug or illicit drug abuse, participant dissatisfaction at any stage of the study, BP < 90, HR < 50, conduction block in ECG) were excluded from the study.

Demographic and laboratory information before the operation was recorded in the data collection form. All three groups of patients underwent a standard treatment with the same anesthesia method (1 mg midazolam + 50 µg fentanyl) with the same treatment group.

At this stage, patients were administered lidocaine (4 cc 2% lidocaine), dexmedetomidine (0.5 g/kgµ dexmedetomidine), and lidocaine + dexmedetomidine (4 cc 2% lidocaine + 0.5 g/kgµ dexmedetomidine) groups. The results from the patients were collected at different time intervals, and the results were analyzed.

Statistical analysis

All quantitative variables were expressed as mean and standard deviation, and qualitative variables were expressed as number (percentage). The Kolmogorov–Smirnov test, box diagrams, and the probability of normal evaluated the normality of quantitative variables. Student's t-test and the Mann–Whitney nonparametric test were used to compare quantitative variables between the two groups. All statistical tests were performed in two domains with a significance level of 5% and will be used to analyze SPSS 21 software (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp).

Results

In this randomized clinical trial, 150 patients with a mean age of 57.2±16.32 were evaluated in three equal groups. Based on the results in (Table 1), no significant differences were observed between the demographic indicators of the patients in the three groups $p>0.05$.

Examination of the hemodynamic status of the patients studied did not show any significant differences between the evaluated indicators in the patients of the three groups ($p>0.05$) (Table 2).

The clinical status of the patients showed that the patients in the combined use of dexmedetomidine and lidocaine group underwent sedation significantly more than the other two groups. However, according to the results of (Table 3), the incidence of cough in this group of patients was significantly lower than in the other groups. An examination of patient satisfaction in different groups shows that the level of satisfaction in the group using a combination of dexmedetomidine and lidocaine was higher than in the other groups (Figure 2).

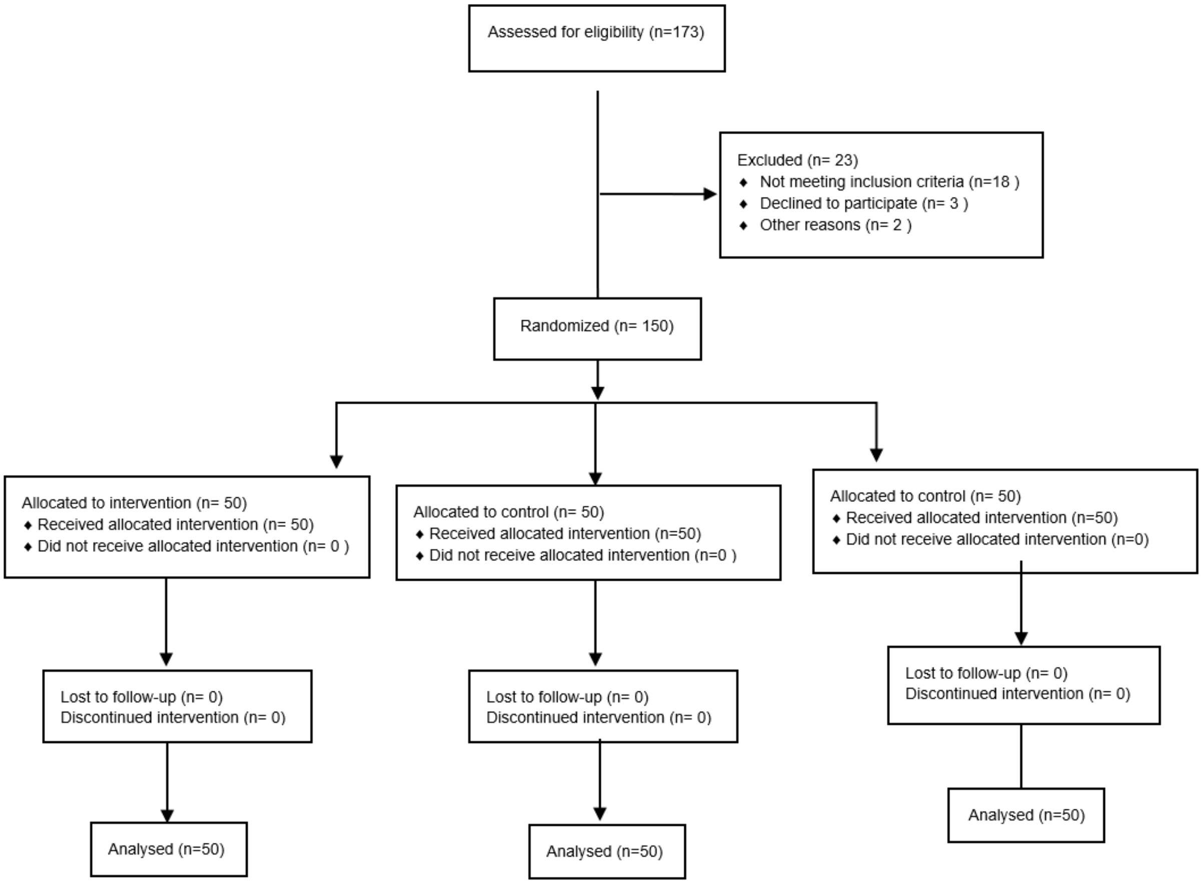

Figure 1- Flowchart of patients participating in the study

Table 1- Demographic information of patients in the study, divided into groups studied.

		Dex Group (Mean± S.D)	Lido Group (Mean± S.D)	Dex+Lido Group (Mean± S.D)	P value
Age (year)		57.14±14.535	59.64±16.718	54.82±17.625	0.361
Gender (MALE)		13 (59.09%)	13(59.09%)	11 (50.0%)	0.513
Weight (kg)		69.32±10.422	69.50±7.999	69.36±16.022	0.227
Height (cm)		167.00±7.044	168.45±5.902	165.68±7.656	0.304
BMI (kg/m^2)		24.93±2.21	24.64±2.67	25.5±2.96	0.181
Underlying disease	Asthma	16(32.00%)	11(22.00%)	18(22.00%)	-
(n (%))	HTN	23 (46.00%)	18 (36.00%)	32 (64.00%)	
	DM	7 (14.00%)	11(22.00%)	14 (28.00%)	
	IHD	4 (8.00%)	0(0.00%)	7(14.00%)	

Table 2- Comparative study of hemodynamic indicators of patients in the study, divided into groups.

	Dex Group Mean± S.D	Lido Group Mean± S.D	Dex+Lido Group Mean± S.D	P value
time p	17.50±6.857	14.32±5.186	18.10±8.136	0.064
MAP1	102.32±8.515	96.73±7.542	104.05±10.366	0.058
MAP2	105.95±6.708	105.59±6.688	101.19±10.458	0.097
HR	92.50±13.862	84.68±7.810	92.33±14.182	0.066
HR2	87.32±11.741	99.27±9.458	86.71±11.675	0.54

Spo_21	94.86±3.771	93.14±3.091	94.95±3.840	0.116
spo_22	94.27±2.914	92.41±2.702	92.95±3.801	0.109
timeR	24.64±8.867	25.77±7.451	26.43±14.675	0.096

Table 3- Comparative study of clinical indicators of patients in the study by groups studied.

		Dex Group	Lido Group	Dex+Lido Group	P value
sedation		2 (9.09%)	4(18.18%)	6 (27.27%)	0.042
Cough	1	8 (36.36%)	4 (18.18%)	5(22.72%)	0.002
	2	9 (40.90%)	11 (50.00%)	1 (4.54%)	
	3	5(22.72%)	7 (31.81%)	0 (0.00%)	
Sore throat		3 (13.63%)	0 (0.00%)	1(4.54%)	0.103
Consent		14 (63.63%)	13 (59.09%)	17 (77.27%)	0.110

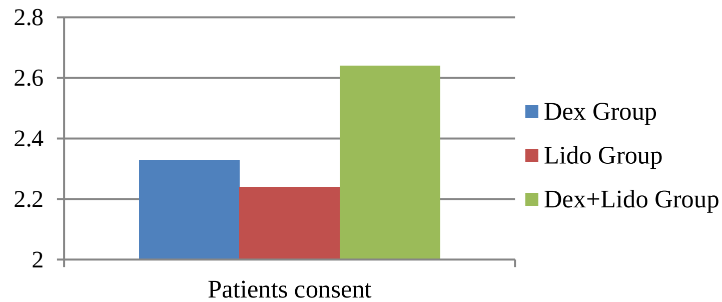

Figure 2- An examination of patient satisfaction in the different study groups

Discussion

Based on the results of the present study, the simultaneous use of lidocaine and transtracheal dexmedetomidine significantly reduces the incidence of cough in patients undergoing bronchoalveolar lavage.

The exact mechanism of cough is unknown, but the proposed mechanism is the excitation of sensory C-fibres and secondary neuroplasticity [25]. The mechanism for cough suppression with lidocaine is yet to be completely understood. Still, various mechanisms to explain the cough suppression by lidocaine include desensitizing peripheral cough receptor suppression of sensory C-fibers and reducing the release of neuropeptides [25-27]. Given the half-life of lidocaine (approximately 2 hours), its inhibitory effect on the cough response can persist until the end of the surgical procedure in short-term surgeries [28, 29]. Lidocaine is an amide anesthetic that plays a significant role in reducing or controlling moderate to severe cough after recovery from anesthesia. A review by Lam et al. [30], which examined 19 studies, showed that in patients undergoing endotracheal intubation who were given intracuff lidocaine to relieve their cough response, the severity of sore throat and cough was significantly lower than in the control group. In line with this study, the results of Tung et al. [31] showed that the use of topical and intracuff lidocaine significantly reduced the incidence and severity of cough after recovery from anesthesia compared with placebo. However, some studies have reported minor side effects such as delayed return to consciousness in patients using this drug [32, 33]. However, in studies that used the recommended dose of lidocaine (1 to 2 mg per kilogram), no significant side effects were observed [34]. The sedative effect of dexmedetomidine has been confirmed in various studies and its role in reducing inflammation, relieving pain, and improving sleep in surgical patients has been identified [35, 36]. Miao et al. [37], in a meta-analysis of 9 studies, confirmed the successful performance of this drug in improving postoperative nausea and vomiting and increasing the quality of recovery. In addition, Wang et al. [38], by examining the appropriate dose of dexmedetomidine, showed that the use of doses of 0.5 and 0.6 μg per kg can improve the cough response and sleep quality of patients. However, these researchers also reported a delay in extubation of this group of patients compared to the control group (administered saline) in patients undergoing endovascular interventions. A study of the efficacy of dexmedetomidine in patients undergoing non-cardiac surgery has shown that its use significantly improves postoperative sleep disorders [39]. Dexmedetomidine can also be used as an adjunct to other anesthetic agents [40]. Yang et al. [41] in a meta-analysis showed that dexmedetomidine administration can play a significant role in reducing patient disorders during recovery from anesthesia and significantly reduce patient restlessness and agitation. Despite the positive effect of dexmedetomidine in relieving pain and improving the recovery process of patients undergoing surgery, the recovery time and tracheal extubation were longer compared to the control group administered saline. Another side effect reported in some studies for dexmedetomidine is a decrease in the patient's level of consciousness and drowsiness. The study by Kim et al. [42] showed that the use of this drug caused a decrease in the level of consciousness of patients compared to the control group. However, in the study by Aouad et al. [35], no difference was observed in the level of consciousness and drowsiness of patients receiving dexmedetomidine compared to other patients. So far, few studies have investigated the side effects of these drugs and the performance of hemodynamic indices. Therefore, it is difficult to investigate the basic mechanisms involved in the occurrence of these side effects. The role of dexmedetomidine in inhibiting the sympathetic nervous system (SNS) and improving tachycardia and reducing blood pressure in patients undergoing extubation has been previously confirmed [43-44]. Aouad et al. [35], while confirming the performance of dexmedetomidine at an optimal dose of 1 μg/kg in improving the quality of recovery after anesthesia, showed that this drug can significantly reduce the severity of cough and restlessness in patients. These researchers also showed that dexmedetomidine reduces blood pressure in patients undergoing general anesthesia. In this regard, Jessen Lundorf et al. [45] reviewed 7 clinical trials and showed that dexmedetomidine can cause a decrease in blood pressure in patients undergoing abdominal surgery. Demiri et al. [46] also confirmed the effectiveness of this drug in reducing heart rate and blood pressure in a systematic review.

Conclusion

The combination of transtracheal lidocaine and dexmedetomidine reduces cough reflex in patients undergoing bronchoscopy and bronchoalveolar lavage without causing adverse hemodynamic effects. However, due to the limited sample size, further studies could be beneficial.

References

[1] Irwin RS. Complications of cough. Chest. 2006;1291:54S–8S.
[2] Francis CK, Singh JB, Polansky BJ. Interruption of aberrant conduction of atrioventricular junctional tachycardia by cough. N Engl J Med. 1972;2867:357–8.
[3] Kim HJ, Kim JS. A cardiovascular collapse following vigorous cough during spinal anesthesia. Korean J Anesthesiol. 2013;656(Suppl):S49–50.
[4] Benedict EB. Rupture of the bronchus from bronchoscopy during a paroxysm of coughing. JAMA. 1961;178:509–10.
[5] Choi EK, Kwon N, Park SJ. Comparison of the effects of oxycodone versus fentanyl on airway reflex to tracheal extubation and postoperative pain during anesthesia recovery after laparoscopic cholecystectomy: A double-blind, randomized clinical consort study. Medicine. 2018;9713:e0156.
[6] Clivio S, Putzu A, Tramèr MR. Intravenous lidocaine for the prevention of cough. AnesthAnalg. 2019;1295:1249–55.
[7] Liu Y, Ai D, Wang X. Efficacy of perioperative intravenous dexmedetomidine administration for the prevention of postoperative sore throat: A meta-analysis. J Int Med Res. 2021;495:3000605211017686.
[8] Mahjoubifard M, Heidari M, Dahmardeh M, Mirtajani SB, Jahangirifard A. Comparison of dexmedetomidine, lidocaine, and fentanyl in attenuation hemodynamic response of laryngoscopy and intubation in patients undergoing cardiac surgery. Anesthesiology research and practice. 2020;2020:4814037.
[9] Sun L, Guo R, Sun L. The impact of prophylactic intravenous lidocaine on opioid-induced cough: A meta-analysis of randomized controlled trials. J Anesth. 2014;283:325–33.
[10] Fan X, Cai H, Pan B, Xie Y. Comparison of dexmedetomidine and remifentanil on reducing coughing during emergence from anesthesia with tracheal intubation: A meta-analysis. Front Pharmacol. 2022;13:993239. doi: 10.3389/fphar.2022.993239.
[11] Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. Int J Surg. 2010;85:336–41.
[12] Minogue SC, Ralph J, Lampa MJ. Laryngotracheal topicalization with lidocaine before intubation decreases the incidence of coughing on emergence from general anesthesia. AnesthAnalg. 2004;994:1253–7.
[13] Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: A revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. doi: 10.1136/bmj.l4898.
[14] Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327:557–60.
[15] Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics. 1994;504:1088–101.
[16] Guyatt GH, Oxman AD, Santesso N, Helfand M, Vist G, Kunz R, et al. GRADE guidelines: 12. Preparing summary of findings tables-binary outcomes. J Clin Epidemiol. 2013;662:158–72.
[17] Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: Is blinding necessary? Control Clin Trials. 1996;171:1–12.
[18] Kothari D, Tandon N, Singh M, Kumar A. Attenuation of circulatory and airway responses to endotracheal extubation in craniotomies for intracerebral space occupying lesions:

Dexmedetomidine versus lignocaine. Anesth Essays Res. 2014;81:78–82.

[19] Mahjoubifard M, Heidari M, Dahmardeh M, Mirtajani SB, Jahangirifard A. Comparison of dexmedetomidine, lidocaine, and fentanyl in attenuation hemodynamic response of laryngoscopy and intubation in patients undergoing cardiac surgery. Anesthesiol Res Pract. 2020;4814037.

[20] Gosai N, Jansari A, Solanki R, Patel D, Prajapati D, Patel B. A comparative study of the effect of dexmedetomidine and lignocaine on hemodynamic responses and recovery following tracheal extubation in patients undergoing intracranial surgery. Int J Basic Clin Pharmacol. 2015;42:371.

[21] Asgari S, Behnaz F, Ommi D, Zandpazandi S, Eraghi MM. The effect of Dexmedetomidine on suppression of the bispectral index score and hemodynamic response during laryngoscopy and intubation in addicted patients in supratentorial brain tumor surgery, a randomized double-blinded controlled trial. Trends Anaesth Crit Care. 2023;53:101293.

[22] Hu S, Li Y, Wang S, Xu S, Ju X, Ma L. Effects of intravenous infusion of lidocaine and dexmedetomidine on inhibiting cough during the tracheal extubation period after thyroid surgery. BMC Anesthesiol. 2019;191:66.

[23] Pradhan A, Pandey A, Kumar Nayak L. To compare the effects of intravenous dexmedetomidine and lignocaine on hemodynamic responses and airway reflexes during tracheal extubation in patients undergoing laparoscopic surgeries. Int J Health Clin Res. 2021;410:1–6.

[24] Safneedha VS. Dexmedetomidine versus Lignocaine for extubation in patients undergoing craniotomies. Indian J Clin Anaesth. 2021;82:326–30.

[25] Burki NK, Lee LY. Blockade of airway sensory nerves and dyspnea in humans. Pulm Pharmacol Ther. 2010;234:279–82.

[26] Tanelian DL, MacIver MB. Analgesic concentrations of lidocaine suppress tonic A-delta and C fiber discharges produced by acute injury. Anesthesiology. 1991;745:934–6.

[27] Woolf CJ, Wiesenfeld-Hallin Z. The systemic administration of local anaesthetics produces a selective depression of C-afferent fibre evoked activity in the spinal cord. Pain. 1985;234:361–74.

[28] Ochs HR, Knüchel M, Abernethy DR, Greenblatt DJ. Dose-independent pharmacokinetics of intravenous lidocaine in humans. J Clin Pharmacol. 1983;234:186–8.

[29] Estebe JP. Intravenous lidocaine. Best Pract Res ClinAnaesthesiol. 2017;314:513–21.

[30] Lam F, Lin YC, Tsai HC, Chen TL, Tam KW, Chen CY. Effect of intracuff lidocaine on postoperative sore throat and the emergence phenomenon: A systematic review and meta-analysis of randomized controlled trials. PLoS One. 2015;108:e0136184. doi: 10.1371/journal.pone.0136184.

[31] Tung A, Fergusson NA, Ng N, Hu V, Dormuth C, Griesdale DEG. Medications to reduce emergence coughing after general anaesthesia with tracheal intubation: A systematic review and network meta-analysis. Br J Anaesth. 2020

[32] Bang SR, Ahn HJ, Kim HJ, Kim GH, Kim JA, Yang M, et al. Comparison of the effectiveness of lidocaine and salbutamol on coughing provoked by intravenous remifentanil during anesthesia induction. Korean J Anesthesiol. 2010;595:319–22.

[33] Mikawa K, Nishina K, Takao Y, Shiga M, Maekawa N, Obara H. Attenuation of cardiovascular responses to tracheal extubation: Comparison of verapamil, lidocaine, and verapamil-lidocaine combination. AnesthAnalg. 1997;855:1005–10.

[34] Rosenberg PH, Veering BT, Urmey WF. Maximum recommended doses of local anesthetics: A multifactorial concept. RegAnesth Pain Med. 2004;296:564–75.

[35] Aouad MT, Zeeni C, Al Nawwar R, Siddik-Sayyid SM, Barakat HB, Elias S, et al. Dexmedetomidine for improved quality of emergence from general anesthesia. AnesthAnalg. 2019;1296:1504–11.

[36] Kim DJ, Kim SH, So KY, Jung KT. Effects of dexmedetomidine on smooth emergence from anaesthesia in elderly patients undergoing orthopaedic surgery. BMC Anesthesiol. 2015;151:139. doi: 10.1186/s12871-015-0127-4.

[37] Miao M, Xu Y, Li B, Chang E, Zhang L, Zhang J. Intravenous administration of dexmedetomidine and quality of recovery after elective surgery in adult patients: A meta-analysis of randomized controlled trials. J Clin Anesth. 2020;65:109849. doi: 10.1016/j.jclinane.2020.109849.

[38] Wang W, Huo P, Wang E, Song W, Huang Y, Liu Z, et al. Dexmedetomidine infusion for emergence coughing prevention in patients undergoing an endovascular interventional procedure: A randomized dose-finding trial. Eur J Pharm Sci. 2022;177:106230.

[39] Duan G, Wang K, Peng T, Wu Z, Li H. The effects of intraoperative dexmedetomidine use and its different dose on postoperative sleep disturbance in patients who have undergone non-cardiac major surgery: A real-world cohort study. Nat Sci Sleep. 2020;12:209–19.

[40] Pandharipande P, Ely E, Maze M. Alpha-2 agonists: Can they modify the outcomes in the postanesthesia care unit? Curr Drug Targets. 2005;67:749–54.

[41] Yang X, Hu Z, Peng F, Chen G, Zhou Y, Yang Q, et al. Effects of dexmedetomidine on emergence agitation and recovery quality among children undergoing surgery under general anesthesia: A meta-analysis of randomized controlled trials. Front Pediatr. 2020;8:580226. doi: 10.3389/fped.2020.580226.

[42] Kim SY, Kim JM, Lee JH, Song BM, Koo BN. Efficacy of intraoperative dexmedetomidine infusion on emergence agitation and quality of recovery after nasal surgery. Br J Anaesth. 2013;1112:222–8.

[43] Kamibayashi T, Maze M, Weiskopf RB, Weiskopf RB, Todd MM. Clinical uses of α2-adrenergic agonists. Anesthesiology. 2000;935:1345–9.

[44] Szumita PM, Baroletti SA, Anger KE, Wechsler ME. Sedation and analgesia in the intensive care unit: Evaluating the role of dexmedetomidine. Am J Health Syst Pharm. 2007;641:37–44.

[45] Jessen Lundorf L, KorveniusNedergaard H, Møller AM. Perioperative dexmedetomidine for acute pain after abdominal surgery in adults. Cochrane Database of Systematic Reviews. 2016;22:CD010358.

[46] Demiri M, Antunes T, Fletcher D, Martinez V. Perioperative adverse events attributed to α2-adrenoceptor agonists in patients not at risk of cardiovascular events: Systematic review and meta-analysis. Br J Anaesth. 2019;1236:795–807