

# Efficacy of intracuff lidocaine in reducing coughing on tube: a systematic review and meta-analysis

Journal of International Medical Research

48(2) 1–12

© The Author(s) 2020

Article reuse guidelines:

[sagepub.com/journals-permissions](http://sagepub.com/journals-permissions)

DOI: 10.1177/0300060520901872

[journals.sagepub.com/home/imr](http://journals.sagepub.com/home/imr)



Fei Peng<sup>1</sup>, Maohua Wang<sup>2</sup>, Huihuang Yang<sup>3</sup>,  
Xiaoli Yang<sup>1</sup> and Menghong Long<sup>1</sup>

## Abstract

**Objective:** To investigate the efficacy of intracuff lidocaine in reducing coughing and other endotracheal tube side effects and so ensure a smooth extubation process.

**Method:** PubMed, EMBASE, and Cochrane Library databases were systematically searched for all randomised controlled trials (RCTs) published before June 30, 2019 that investigated the efficacy of intracuff lidocaine, with or without sodium bicarbonate, in reducing coughing and other complications related to endotracheal intubation. A random-effects model was used to conduct a meta-analysis to assess the relative risks (RRs) of the incidence of these intubation-related side effects.

**Results:** 11 studies involving 843 patients were included in the meta-analysis. Compared with control groups (i.e., saline or air), intracuff lidocaine groups (alkalinized or non-alkalinized) had a significantly reduced incidence of coughing on tube. Similarly, intracuff lidocaine groups were more effective than control groups in reducing the incidence of other intubation-related complications.

**Conclusion:** Intracuff alkalinized or non-alkalinized lidocaine significantly reduced coughing and other intubation-related complications during the extubation process.

## Keywords

Endotracheal tube, coughing, dysphonia, hoarseness, agitation, lidocaine, sodium bicarbonate, meta-analysis

Date received: 24 July 2019; accepted: 8 October 2019

<sup>1</sup>Southwest Medical University, Luzhou, Sichuan Province, China

<sup>2</sup>Department of Anesthesiology, The Affiliated Hospital of Southwest Medical University, Luzhou, Sichuan Province, China

<sup>3</sup>Guangdong Medical University, Zhanjiang, Guangdong Province, China

## Corresponding author:

Maohua Wang, Department of Anesthesiology, The Affiliated Hospital of Southwest Medical University, Luzhou, Sichuan Province, China.  
Email: [wangmaohua@swmu.edu.cn](mailto:wangmaohua@swmu.edu.cn)



## Introduction

Endotracheal intubation is the most commonly used airway management method during general anaesthesia because it is safe for the patients and convenient for the anaesthetists. Moreover, the use of a cuffed tube protects the lungs from aspiration of stomach contents and importantly, also prevents positive pressure ventilation due to leakage. The procedure involves insertion of a plastic or hard metal laryngoscope into the patient's mouth followed by a series of manipulations including lifting of the epiglottis and then placement of the endotracheal tube (ETT) into the patient's trachea between the V-shaped vocal cords. These manipulations in the patient's mouth can cause transient irritation to the local mucosa of the oropharynx or trachea.<sup>1</sup> In addition, several studies have reported that during inhalational anaesthesia with nitrous oxide (N<sub>2</sub>O), diffusion of the gas into the ETT cuff can increase the cuff pressure which can also induce tracheal mucosal injury.<sup>2,3</sup> These injuries can influence the extubation process and be responsible for complications such as excessive coughing or bucking on tube. Indeed, coughing induced by the ETT can be dangerous because it can cause increased cerebral pressure, intraocular pressure, intraabdominal and/or systemic blood pressure which may result in myocardial ischemia, surgical bleeding, tachycardia, bronchospasm and other life-threatening complications.<sup>4-6</sup>

A number of methods have been used to reduce complications during the extubation process such as intravenous drugs or extubation under deep anaesthesia.<sup>4,7,8</sup> However, these methods may themselves cause complications, such as general anaesthesia-delayed awakening.<sup>4</sup> The use of a topical local anaesthetic during the extubation process has been suggested as a possible

alternative that may act to suppress cough while preventing delayed awakening.<sup>9,10</sup> One of the methods used to apply local anaesthetic to the mucosa uses an intracuff injection of lidocaine.<sup>11,12</sup> In addition to providing a local anaesthetic effect and suppressing complications during extubation, it also prevents diffusion of inhalational anaesthetics into the ETT cuff.<sup>11,13,14</sup> Furthermore, the addition of sodium bicarbonate (NaHCO<sub>3</sub>) (i.e., alkalinisation) increases diffusion across the cuff and enables low doses of lidocaine to be used effectively.<sup>10</sup>

To our knowledge, no systematic review has been performed to evaluate the efficacy of intracuff lidocaine on preventing ETT-related cough on tube. Therefore, we conducted a systematic review and meta-analysis according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) regulations<sup>15</sup> to evaluate the efficacy of intracuff lidocaine in reducing cough on tube and some other common ETT side effects during the extubation process.

## Methods

The Cochrane Library, PubMed and EMBASE databases were systematically searched for randomized controlled clinical trials (RCTs) published before June 30, 2019 that investigated the use of intracuff alkalinized or non-alkalinized lidocaine for the prevention of cough on tube and other intubation-related complications (i.e., hoarseness, agitation, restlessness, dysphonia) on extubation. In addition, the reference lists of all included studies were checked for any potential additional publications. Key words/terms in both AND and OR combinations included: lidocaine; lignocaine; xylocaine; coughing; hoarseness; dysphonia; agitation; restlessness;

emergency; general anaesthesia; endotracheal tube; extubation.

For a published report to be included in the meta-analysis, it had to fulfil the following criteria: (1) be a RCT; (2) be an English language article; (3) have investigated the efficacy of intracuff lidocaine for reducing coughing on tube and other intubation-related complications on extubation. Studies with small sample sizes and those with emergency operations were excluded as were duplicate publications, reviews, editorials, abstracts, comments, case reports, meetings and those involving animals. Two reviewers [F.P., H.Y.] independently screened the papers from their titles and abstracts and selected relevant studies. The same two reviewers [F.P., H.Y.] independently extracted data from the studies according to a prespecified protocol with any disagreement settled by a third reviewer [M.W.].

The following items were extracted: name of the first author; publication year; country; type of surgery; American Society of Anaesthesiologists (ASA) status;<sup>16</sup> sample size; sex; age; tube size; anaesthetic; ETT intervention; incidence of coughing, hoarseness, agitation/restlessness, and dysphonia related to ETT during the extubation process).

The primary outcome of the meta-analysis was the incidence of coughing on tube. The secondary outcome was the incidences of hoarseness, agitation/restlessness and dysphonia during the extubation process. Control groups included patients with intracuff saline or intracuff air. Patients were separated into two subgroups based on if they had received NaHCO<sub>3</sub> with the lidocaine (i.e., 'alkalinized lidocaine' or 'non-alkalinized lidocaine').

The study was approved by the Ethics Committee of the Affiliated Hospital of Southwest Medical University, Luzhou, China and because this was a meta-analysis of previously published articles, ethical approval was not required.

### Statistical analyses

The meta-analysis was performed using Review Manager (RevMan) [Computer program] Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014 and a sensitivity analysis was performed using the soft-ware package Stata version12 (Stata Corp, College Station, Texas). A  $P$ -value  $<0.05$  was considered to indicate statistical significance.

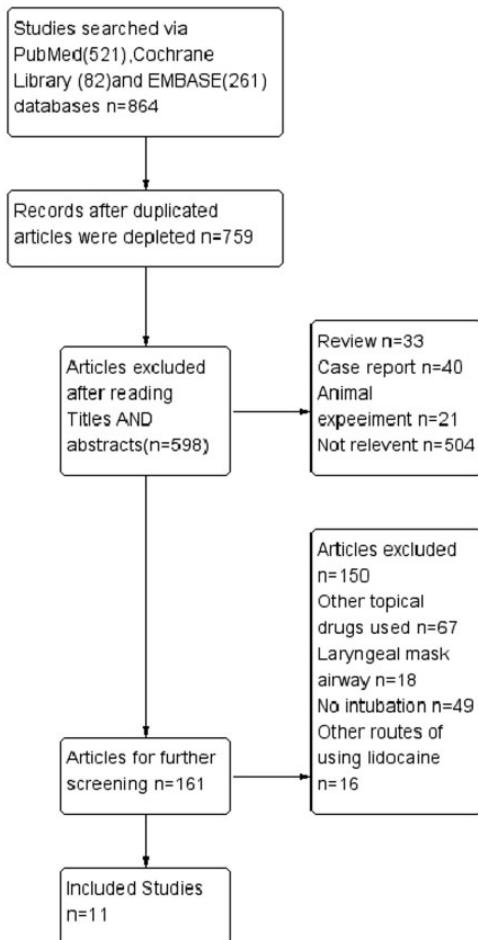
The level of evidence quality of each study was estimated according to the guidelines of Grading of Recommendations, Assessment, Development, and Evaluation (GRADE).<sup>17</sup> The GRADE approach applies a sequential assessment of the evidence quality and a subsequent judgment on the strength of the recommendations. The evidence grades were classified into four categories: (1) high grade (further research is unlikely to change confidence in the effect estimate); (2) moderate grade (further research is likely to alter confidence in the effect estimate and may change the estimate); (3) low grade (further research is very likely to alter confidence in the effect estimate significantly and to change the estimate); (4) very low grade (any effect estimate is uncertain). Cochran's  $Q$  test and Higgins'  $I^2$  statistical test were used to assess the statistical heterogeneity of the pooled results. If  $I^2$  statistic  $\geq 50\%$  and  $P < 0.05$ , a random effects model was applied to the data. If no heterogeneity was observed, a fixed effect model was to be used.

Data were pooled from all eligible RCTs and the Mantel-Haenszel method was used to calculate the risk ratio (RR) with 95% CIs for these dichotomous outcomes. A pooled estimate of RR was computed using the DerSimonian and Laird random-effects model.<sup>18,19</sup> This model provides an appropriate estimate of the average treatment effect when studies are

statistically heterogeneous, and it typically yields relatively wide CIs resulting in a more conservative statistical claim. In addition, a sensitivity analysis was used to assess the robustness of the results and Begg's funnel plot was used to assess potential publication bias.

## Results

The literature search identified 864 articles from which 11 articles ultimately met the eligibility criteria (Figure 1). The main



**Figure 1.** Flow diagram of included and excluded studies.

features of the 11 studies that involved 843 patients are summarized in Table 1. Of the 11 studies, three were performed in France, two in India and one in each of the following countries: Canada; Kingdom of Saudi Arabia; Brazil, Turkey; Tunisia; Ireland. With the exception of one study in children,<sup>21</sup> all studies involved adult patients.

By comparison with controls, prevention of intubation-related complications was investigated in eight studies using intracuff alkalized lidocaine<sup>10,20–26</sup> and four studies using intracuff non-alkalinized lidocaine.<sup>12,26–28</sup> In addition, one controlled study included the effects of intracuff alkalized lidocaine and intracuff non-alkalinized lidocaine.<sup>26</sup> With the exception of two studies, one that used 4% lidocaine<sup>28</sup> and the other 10% lidocaine,<sup>12</sup> all studies used 2% lidocaine instilled into the endotracheal tube cuff. Six studies used 8.4% NaHCO<sub>3</sub><sup>10,20,21,24–26</sup> two studies used 7.5% NaHCO<sub>3</sub><sup>22,23</sup> and one study included a subgroup who received 1.4% NaHCO<sub>3</sub>.<sup>20</sup>

Eight studies used endotracheal tube cuffs inflated with saline as control,<sup>10,12,21–24,27,28</sup> six studies used cuffs injected with air as control,<sup>20,22,23,25,26,28</sup> and three studies used both saline and air as control.<sup>22,23,28</sup> In addition, five studies investigated the additional use of lubricants on the tube cuff (i.e., lidocaine, saline or water-soluble gel)<sup>20,23–26</sup> and two studies investigated the effects of additional sprays on the larynx (i.e., 2% lidocaine or saline).<sup>10,27</sup>

There were differences between studies in anaesthetic techniques. For example, six studies<sup>20,21,23–25,28</sup> premedicated their patients and N<sub>2</sub>O was administered for anaesthesia maintenance in seven studies.<sup>12,22–26,28</sup> All of these differences contributed to the statistical heterogeneity of the studies.

In terms of the primary outcome, the incidence of coughing on tube, the aggregate outcome of the 11 studies favoured

**Table 1.** Characteristics of the 11 randomized controlled clinical trials included in the meta-analysis investigating the efficacy of intracuff lidocaine in reducing coughing and other endotracheal tube side effects.

Study	Country	N (M/F)	Age (y)	Surgery (ASA status)	Tube size (mm)	Anaesthetic		Endotracheal tube intervention				
						Premedication	Induction	Maintenance	Alkalinized Lidocaine*	Non Alkalinized Lidocaine <sup>z</sup>	Saline	Air
D'Aragon et al. (2013) <sup>10</sup>	Canada	116 (0/116)	Mean 44	Gynaecological (I-II)	7	NR	Fentanyl, propofol, rocuronium	50% O <sub>2</sub> , desflurane, fentanyl, rocuronium	30 <sup>#</sup> /28 <sup>#</sup>	29 <sup>#</sup> /29 <sup>#</sup>	–	–
Estebe et al. (2005) <sup>20</sup>	France	60(13/47)	Mean 48	Thyroidectomy (I-II)	M = 7–7.5 F = 6.5–7	Alprazolam	Propofol, sufentanil, atracurium	50% O <sub>2</sub> , 50% air, sevoflurane, sufentanil	20 <sup>i</sup> /20 <sup>β,λ</sup>	–	–	20 <sup>λ</sup>
Ahmady et al. (2013) <sup>21</sup>	KSA	50 (31/19)	Mean 8	Dental (I-II)	Age/4+ 3	Diazepam	Fentanyl, propofol, rocuronium	50% O <sub>2</sub> , sevoflurane, fentanyl	25	25	25	–
Shroff & Patil (2009) <sup>22</sup>	India	150 (51/99)	Mean 37	Elective (I-II)	NR	NR	Opioid, propofol, benzodiazepine, non-depolarizing muscle relaxant.	60%N <sub>2</sub> O	50 <sup>γ</sup>	50	50	50
Jaichandran et al. (2009) <sup>23</sup>	India	75 (61/14)	Mean 32	Eye (I-II)	M = 8–8.5 F = 7–7.5	Glycopyrrolate and pentazocine	Propofol, vecuronium	70% N <sub>2</sub> O, isoflurane, vecuronium	25 <sup>γ,δ</sup>	25 <sup>δ</sup>	25 <sup>δ</sup>	25 <sup>δ</sup>
Navarro et al. (2012) <sup>24</sup>	Brazil	50 (13/37)	> 18	Gynaecological/ orthopaedic/ plastic (I-II)	M = 8 F = 7.5	Midazolam	NR	60% N <sub>2</sub> O, isoflurane, sufentanil, rocuronium	25 <sup>δ</sup>	25 <sup>δ</sup>	25 <sup>δ</sup>	25 <sup>δ</sup>
Estebe et al. (2004) <sup>25</sup>	France	60 (39/21)	Mean 50	Spinal (I-III)	M = 7–7.5 F = 6.5–7	Hydroxyzine	Thiopental, sufentanil, rocuronium	70% N <sub>2</sub> O, isoflurane, sufentanil, rocuronium	20 <sup>i</sup> /20 <sup>δ</sup>	–	–	20 <sup>λ</sup>
Estebe et al. (2002) <sup>26</sup>	France	75 (40/35)	Mean 46	Spinal (I-III)	NR	NR	Standard anaesthetics	70%N <sub>2</sub> O, isoflurane, sufentanil, rocuronium	25 <sup>λ</sup>	–	–	25 <sup>λ</sup>

(continued)

Table I. Continued

Study	Country	N (M/F)	Age (y)	Surgery (ASA status)	Tube size (mm)	Anaesthetic			Endotracheal tube intervention			
						Premedication	Induction	Maintenance	Alkalinized Lidocaine <sup>*</sup> n	Non alkalinized Lidocaine <sup>*</sup> n	Saline n	Air n
Altintas et al. (2000) <sup>12</sup>	Turkey	70 (31/39)	Mean 30	Plastic (I-II)	M = 8 F = 7	None	Fentanyl, propofol atracurium	50% N <sub>2</sub> O, isoflurane, fentanyl	36 <sup>∞</sup>	34		
Bousselmi et al. (2014) <sup>27</sup>	Tunisia	80 (49/31)	Mean 49	Elective (I-III)	M = 7.5 F = 7	NR	Propofol, remifentanyl, cisatracurium	propofol and remifentanyl, cisatracurium	20 <sup>#</sup> /20 <sup>∞</sup>	20 <sup>#</sup> /20 <sup>∞</sup>		
Fagan et al. (2000) <sup>28</sup>	Ireland	57 (NR)	Mean 40	Orthopaedic/urological/plastic (I-II)	M = 8.5 F = 7.5	Diazepam	Fentanyl, propofol, vecuronium	65% N <sub>2</sub> O, isoflurane, fentanyl	18 <sup>♂</sup>	18		21

Abbreviations: KSA, Kingdom of Saudi Arabia; ASA, American Society of Anaesthesiologists<sup>16</sup>; M, male; F, female; NR, not recorded; N<sub>2</sub>O, nitrous oxide.

<sup>\*</sup>Lidocaine 2%, sodium bicarbonate 8.4% (unless otherwise specified).

<sup>α</sup>Lidocaine 2%.

<sup>β</sup>Lidocaine 2%, sodium bicarbonate 1.4%.

<sup>γ</sup>Lidocaine 2%, sodium bicarbonate 7.5%.

<sup>∞</sup>Lidocaine 10%.

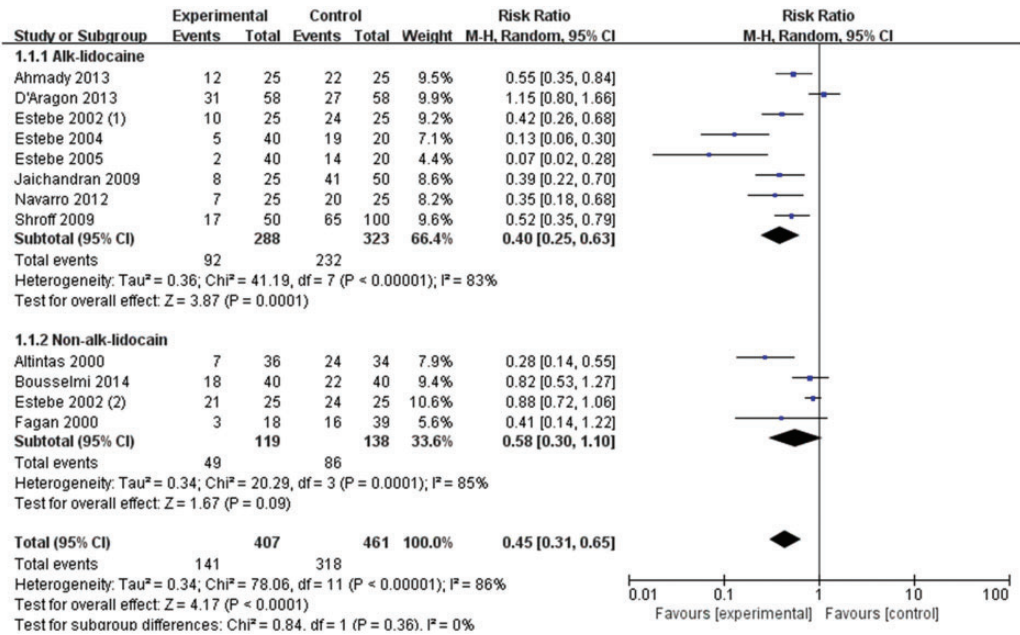
<sup>♂</sup>Lidocaine 4%.

<sup>#</sup>Saline on larynx.

<sup>‡</sup>Lidocaine 2% on larynx.

<sup>‡</sup>Sterile water used as a lubricant on the tracheal tube.

<sup>δ</sup>Water soluble gel used as a lubricant on the tracheal tube.



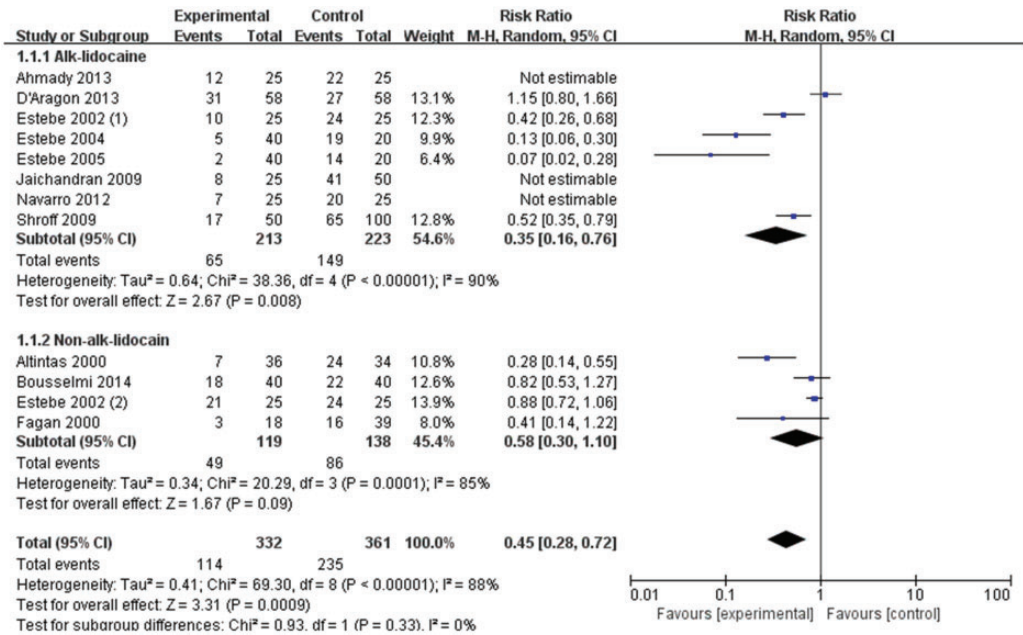
**Figure 2.** Forest plot evaluating the effects of intracuff lidocaine (alkalinized and non-alkalinized) by comparison with control groups (saline or air) on the incidence of coughing during endotracheal tube intubation. Abbreviations: Alk-lidocaine, alkalinized lidocaine; Non-alk-lidocaine, non-alkalinized lidocaine; Estebe 2002 (1) and (2), this study included alkalinized and non-alkalinized groups; M–H, Mantel–Haenszel; df, degrees of freedom; experimental, lidocaine.

the lidocaine groups over the control groups (RR, 0.45; 95% CI, 0.31, 0.65;  $P < 0.0001$ ;  $I^2 = 86\%$ ) (Figure 2). The results of the subgroup analyses showed that by comparison with controls, the application of intracuff alkalinized lidocaine was more effective than that of non-alkalinized intracuff lidocaine in reducing the incidence of coughing on tube (RR: 0.40; 95% CI: 0.25, 0.63;  $P < 0.0001$ ;  $I^2 = 83\%$  and (RR: 0.58; 95% CI: 0.30, 1.10;  $P < 0.0001$ ;  $I^2 = 85\%$ ), respectively) (Figure 2).

The analysis was repeated after excluding three studies that had included high-risk patient groups (i.e., children,<sup>21</sup> smokers<sup>24</sup> and patients with hyperactive airways<sup>23</sup>). There was no significant difference in the outcome; the lidocaine groups were more effective than the control groups in reducing the incidence of coughing on tube (Figure 3).

Studies that assessed hoarseness, agitation/restlessness and/or dysphonia are shown in Table 2. Analysis of the secondary outcome showed that by comparison with controls, intracuff administration of alkalinized lidocaine or non-alkalinized lidocaine produced a significant reduction in the incidence of other intubation-related complications (Table 3)

According to the GRADE recommendations for level of evidence quality, the results from the 11 studies were classed as ‘low grade’.<sup>19</sup> In addition, the results of a Begg’s funnel plot showed asymmetry in the scatter of studies indicating publication bias (Figure 4). However, the results of a sensitivity analysis showed that the omission of each study in the analysis of RRs did not significantly alter the overall results indicating that our pooled analysis from 11 studies was robust (Figure 5).



**Figure 3.** Forest plot evaluating the effects of intracuff lidocaine (alkalinized and non-alkalinized) by comparison with control groups (saline or air) on the incidence of coughing during endotracheal tube intubation after excluding three studies involving high-risk patient groups.<sup>21,23,24</sup>

Abbreviations: Alk-lidocaine, alkalinized lidocaine; Non-alk-lidocaine, non-alkalinized lidocaine; Estebe 2002 (1) and (2), this study included alkalinized and non-alkalinized groups; M-H, Mantel-Haenszel; df, degrees of freedom; experimental, lidocaine.

## Discussion

Although a previous systematic review and meta-analysis has investigated the effects of intracuff lidocaine on postoperative sore throat,<sup>29</sup> no systematic review has previously been performed to evaluate the efficacy of intracuff lidocaine on preventing ETT-related coughing a potentially life-threatening complication which can occur during the extubation process.<sup>4-6</sup>

The results of this meta-analysis of 11 RCTs involving 843 patients showed that the administration of alkalinized or non-alkalinized lidocaine to endotracheal tube cuffs significantly reduced coughing on tube and other intubation-related complications (i.e., hoarseness, agitation/restlessness and/or dysphonia) during the extubation process. In addition, by comparison with

controls, intracuff administration of alkalinized lidocaine tended to be more effective than non-alkalinized lidocaine. Importantly, the outcome was similar when studies with high risk patients (i.e., children, smokers and those with hyperactive airways)<sup>21,23,24</sup> were excluded from the analysis. However, according to GRADE recommendations the studies were classed as 'low level of evidence quality' and results from a funnel plot indicated potential publication bias.

Many different factors in these studies contributed to their heterogeneity. Firstly, the patients' characteristics varied from study to study. For example, one study only included female patients<sup>10</sup> and another only children.<sup>21</sup> In addition, one study focused on patients with hyperactive



**Table 2.** Studies that assessed the efficacy of intracuff lidocaine on the incidence of hoarseness, agitation/restlessness and dysphonia during the extubation process.

Study	Total No. patients	No receiving lidocaine	Hoarseness	Agitation/ Restlessness	Dysphonia
<b>Alkalinized Lidocaine</b>					
D'Aragon et al. (2013) <sup>10</sup>	116	58	X	√	X
Estebe, et al. (2005) <sup>20</sup>	60	40	√	√	√
Ahmady, et al. (2013) <sup>21</sup>	50	25	√	X	X
Shroff & Patil (2009) <sup>22</sup>	150	50	√	√	X
Jaichandran et al. (2009) <sup>23</sup>	75	25	X	X	X
Navarro et al. (2012) <sup>24</sup>	50	25	√	X	X
Estebe, et al. (2004) <sup>25</sup>	60	40	√	√	√
*Estebe, et al. (2002) <sup>26</sup>	75	25	√	√	√
<b>Non-alkalinized Lidocaine</b>					
*Estebe, et al. (2002) <sup>26</sup>	75	25	√	√	√
Altintas, et al. (2000) <sup>12</sup>	70	36	X	X	X
Bousselmi, et al. (2014) <sup>27</sup>	80	40	X	X	√
Fagan et al. (2000) <sup>28</sup>	57	18	X	X	X

\*Estebe et al, 2002 included alkalinized and non- alkalinized groups.

**Table 3** Efficacy of intracuff lidocaine in the reduction of other complications during the extubation process.

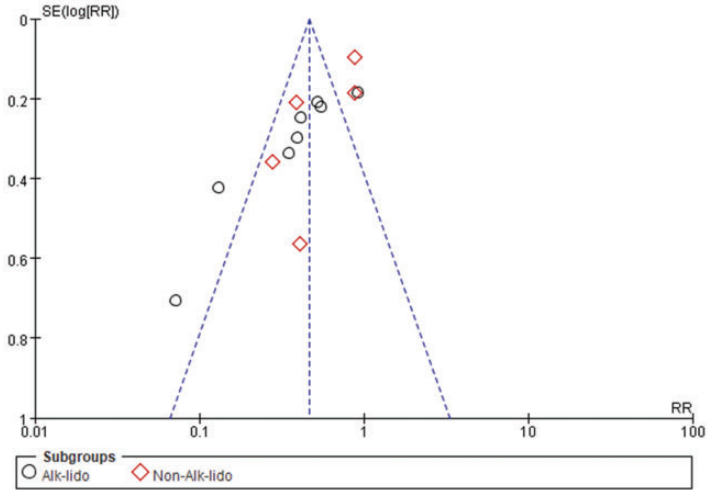
Secondary outcomes	No. Studies	No. patients	Risk ratio (95% CIs)	Statistical significance
Hoarseness (overall)	*6 <sup>20-22,24-26</sup>	445	0.21 (0.02, 1.57)	$P < 0.001$
alkalinized lidocaine	6 <sup>20-22,24-26</sup>	205	0.44 (0.34, 0.57)	$P < 0.01$
non- alkalinized lidocaine	1 <sup>26</sup>	25	0.05 (0.01, 0.36)	$P < 0.01$
Agitation/Restlessness (overall)	*5 <sup>10,20,22,25,26</sup>	461	0.24 (0.17, 0.43)	$P = 0.02$
alkalinized lidocaine	5 <sup>10,20,22,25,26</sup>	213	0.07 (0.02, 0.29)	$P < 0.01$
non- alkalinized lidocaine	1 <sup>26</sup>	25	0.13 (0.02, 0.93)	$P = 0.04$
Dysphonia (overall)	*4 <sup>20,25-27</sup>	275	0.28 (0.14, 0.51)	$P < 0.01$
alkalinized lidocaine	3 <sup>20,25,26</sup>	105	0.16 (0.06, 0.46)	$P < 0.01$
non- alkalinized lidocaine	2 <sup>26,27</sup>	65	0.33 (0.25, 0.51)	$P < 0.0001$

\*Estebe et al, 2002 included alkalinized and non- alkalinized groups.

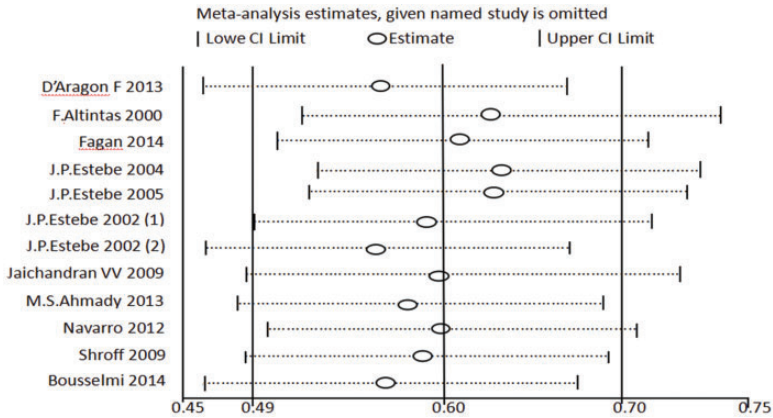
airways<sup>23</sup> and another on smokers.<sup>24</sup> Secondly, patients underwent different types of surgeries and were subjected to various anaesthetic strategies. For instance, the anaesthetic interventions varied in their use of different endotracheal tube sizes, pre-medications, and techniques for maintenance of anaesthesia. Finally, the concentration of lidocaine with or without alkalinisation differed among studies as

did the control groups (i.e., saline or air) and the concentration of NaHCO<sub>3</sub>. Nevertheless, the results of a sensitivity analysis of these data showed that omission of each study did not significantly alter the overall results of this meta-analysis indicating that our findings were not driven by any single study and the analysis was robust.

The study had several limitations. For example, only 11 studies were included in



**Figure 4.** Funnel plot for evaluation of potential publication bias. Abbreviations: Alk-lido, alkalinized lidocaine; Non-alk-lido, non-alkalinized lidocaine; RR, risk ratio; SE, standard error.



**Figure 5.** Sensitivity analysis to confirm the robustness of the results by removing one study at a time. Each circle and dotted line represent the risk ratio (RR) and 95% CIs with the corresponding study omitted from the overall result.

the analysis and of these studies, eight used intracuff alkalinized lidocaine and four intracuff non-alkalinized lidocaine. Although all studies assessed the effects of lidocaine on coughing, few studies assessed the effects of non-alkalinized lidocaine on the other ETT-related complications. Additionally, only one studied included

alkalinized lidocaine and non-alkalinized lidocaine groups. Moreover, the sample sizes in all studies were small. Furthermore, all studies in this analysis were classed as 'low quality' according to GRADE recommendations and the funnel plot indicated publication bias. Therefore, more prospective, controlled,

comparative studies involving large numbers of patients are required to confirm these results.

In summary, the results of this meta-analysis suggest that intracuff application of lidocaine, alkalized or non-alkalinized, can be helpful in the prevention of coughing and other intubation-related complications during the extubation process. However, further research is required to confirm these results in both regular and high-risk patient groups.

### Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

### Funding

The study was supported by Sichuan Science and Technology Department Foundation (2019YJ0692), the Joint Foundation of Luzhou Government and Southwest Medical University (2018LZXNYD-ZK02).

### References

- McHardy FE and Chung F. Postoperative sore throat: cause, prevention and treatment. *Anaesthesia* 1999; 54: 444–453.
- Tu HN, Saidi N, Lietaut T, et al. Nitrous oxide increases endotracheal cuff pressure and the incidence of tracheal lesions in anesthetized patients. *Anesth Analg* 1999; 89: 187–190.
- Bernhard WN, Yost LC, Turndorf H, et al. Physical characteristics of and rates of nitrous oxide diffusion into tracheal tube cuffs. *Anesthesiology* 1978; 48: 413–417.
- Gonzalez RM, Bjerke RJ, Drobycki T, et al. Prevention of endotracheal tube-induced coughing during emergence from general anesthesia. *Anesth Analg* 1994; 79: 792–795.
- Stoelting RK. Blood pressure and heart rate changes during short-duration laryngoscopy for tracheal intubation: influence of viscous or intravenous lidocaine. *Anesth Analg* 1978; 57: 197–199.
- Stoelting RK. Circulatory changes during direct laryngoscopy and tracheal intubation: influence of duration of laryngoscopy with or without prior lidocaine. *Anesthesiology* 1977; 47: 381–384.
- Mendel P, Fredman B and White PF. Alfentanil suppresses coughing and agitation during emergence from isoflurane anesthesia. *J Clin Anesth* 1995; 7: 114–118.
- Shajar MA, Thompso JP, Hal AP, et al. Effect of a remifentanil bolus dose on the cardiovascular response to emergence from anesthesia and tracheal extubation. *Br J Anaesth* 1999; 83: 654–656.
- Minogue SC, Ralph J and Lampa MJ. Laryngotracheal topicalization with lidocaine before intubation decreases the incidence of coughing on emergence from general anesthesia. *Anesth Analg* 2004; 99: 1253–1257.
- D'Aragon F, Beaudet N, Gagnon V, et al. The effects of lidocaine spray and intracuff alkalized lidocaine on the occurrence of cough at extubation: a randomized controlled trial. *Can J Anaesth* 2013; 60: 370–376.
- Sconzo JM, Moscicki JC and Difazio CA. In vitro diffusion of lidocaine across endotracheal tube cuffs. *Reg Anesth* 1990; 15: 37–40.
- Altintas F, Bozkurt P, Kaya G, et al. Lidocaine 10% in the endotracheal tube cuff: blood concentrations, haemodynamic and clinical effects. *Eur J Anesthesiol* 2000; 17: 436–442.
- Dollo G, Estebe JP, Le Corre P, et al. Endotracheal tube cuffs filled with lidocaine as a drug delivery system: in vitro and in vivo investigations. *Eur J Pharm Sci* 2001; 13: 319–323.
- Navarro RM and Baughman VL. Lidocaine in the endotracheal tube cuff reduces postoperative sore throat. *J Clin Anesth* 1997; 9: 394–397.
- Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009; 339: b2535.
- Mayhew D, Mendonca V, Murthy BVS. A review of ASA physical status – historical perspectives and modern developments. *Anaesthesia*. 2019 Mar;74(3):373–379.

17. Goldet G, Howick J. Understanding GRADE: an introduction. *J Evid Based Med* 2013; 6:50–54.
18. DerSimonian R and Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; 7: 177–188.
19. IntHout J, Ioannidis JP and Borm GF. The Hartung-Knapp-Sidik-Jonkman method for random effects meta-analysis is straightforward and considerably outperforms the standard DerSimonian-Laird method. *BMC Med Res Methodol* 2014; 14: 25.
20. Estebe JP, Gentili M, Le Corre P, et al. Alkalinization of intracuff lidocaine: efficacy and safety. *Anesth Analg* 2005; 101: 1536–1541.
21. Ahmady MS, Sadek S and Al-metwalli RR. Does intra-cuff alkalinized lidocaine induced emergence phenomena in children? *Anaesth Pain & Intensive Care* 2013; 17: 18–21. [http://applications.emro.who.int/imemrf/Anaesth\\_Pain\\_Intensive\\_Care/Anaesth\\_Pain\\_Intensive\\_Care\\_2013\\_17\\_1\\_18\\_21.pdf](http://applications.emro.who.int/imemrf/Anaesth_Pain_Intensive_Care/Anaesth_Pain_Intensive_Care_2013_17_1_18_21.pdf)
22. Shroff PP and Patil V. Efficacy of cuff inflation media to prevent postintubation-related emergence phenomenon: air, saline and alkalinized lignocaine. *Eur J Anaesthesiol* 2009; 26: 458–462.
23. Jaichandran V, Bhanulakshmi IM and Jagadeesh V. Intracuff buffered lidocaine versus saline or air—a comparative study for smooth extubation in patients with hyperactive airways undergoing eye surgery. *SAJAA* 2009; 15: 11–14. <https://www.tandfonline.com/doi/pdf/10.1080/22201173.2009.10872600?needAccess=true>
24. Navarro LH, Lima RM, Aguiar AS, et al. The effect of intracuff alkalinized 2% lidocaine on emergence coughing, sore throat, and hoarseness in smokers. *Rev Assoc Med Bras* 2012; 58: 248–253.
25. Estebe JP, Delahaye S, Le Corre P, et al. Alkalinization of intra-cuff lidocaine and use of gel lubrication protect against tracheal tube-induced emergence phenomena. *Br J Anaesth* 2004; 92: 361–366.
26. Estebe JP, Dollo G, Le Corre P, et al. Alkalinization of intracuff lidocaine improves endotracheal tube-induced emergence phenomena. *Anesth Analg* 2002; 94: 227–230.
27. Bousselmi R, Lebba MA, Bargaoui A, et al. Lidocaine reduces endotracheal tube associated side effects when instilled over the glottis but not when used to inflate the cuff: a double blind, placebo-controlled, randomized trial. *Tunis Med* 2014; 92: 29–33.
28. Fagan C, Frizelle HP, Laffey J, et al. The effects of intracuff lidocaine on endotracheal-tube-induced emergence phenomena after general anesthesia. *Anesth Analg* 2000; 91: 201–205.
29. Lam F, et al. 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;10:e0136184.