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ABOUT COVER

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AIMS AND SCOPE

The primary aim of World Journal of Clinical Cases (WJCC, World J Clin Cases) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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META-ANALYSIS

Intracuff alkalinized lidocaine to prevent postoperative airway complications: A meta-analysis

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Abstract

BACKGROUND

Post-extubation cough is a common phenomenon in surgical patients undergoing general anesthesia, which can lead to potentially dangerous complications. In this meta-analysis, we evaluated the efficacy and safety of intracuff alkalinized lidocaine in patients with tracheal intubation to prevent cough and other airway complications during the perioperative period.

AIM

To perform a systematic review and meta-analysis of intracuff alkalinized lidocaine for the prevention of postoperative airway complications.

METHODS

PubMed, Embase, Cochrane, and Web of Science were searched for randomized controlled trials (RCTs) that compared intracuff alkalinized lidocaine to placebo. We used risk-of-bias assessment to assess the RCTs, and the quality of evidence was assessed using the grading of recommendations, assessment, development, and evaluations.

RESULTS

Twelve randomized trials (1175 patients) were analyzed. Meta-analysis showed that intracuff alkalinized lidocaine was associated with less cough compared to that produced by placebo [risk ratio (RR): 0.38; 95% confidence interval (CI): 0.23-0.63]. Similarly, intracuff alkalinized lidocaine was more effective than the control in reducing postoperative sore throat at 24 h (RR: 0.19; 95% CI: 0.09-0.41) and postoperative hoarseness (RR: 0.38; 95%CI: 0.21-0.69).

CONCLUSION



Grade E (Poor): 0

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Intracuff alkalinized lidocaine is an effective adjuvant that can decrease airway complications, such as coughing, hoarseness, and sore throat.

Key Words: Cough; Hoarseness; Lidocaine; Sore throat; Airway complication; Intracuff; Meta-analysis

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Core Tip: Our study is different to previous systematic reviews and meta-analysis. We focused on adult patients and included relevant literature on alkalinized lidocaine in the analysis. In addition, this is the first systematic review and meta-analysis to analyze lubrication of the cuff before intubation in order to eliminate the influence of confounding factors on the results.

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INTRODUCTION

Tracheal intubation is the most commonly used airway management method in general anesthesia. Due to its high safety, simple operation, and convenient management, it has become the most important airway management method in most operations[1]. However, this approach has been associated with some problems, such as postoperative airway complications[2], which are common phenomena and adverse reactions in patients who underwent elective general anesthesia. Under normal physiological conditions, cough serves as a protective mechanism, which can clear sputum and foreign matter from the airway and prevent aspiration that may cause pneumonia^[3]. However, after the operation, during recovery from general anesthesia, coughing may cause potentially dangerous complications^[4]. Coughing may lead to increased intracranial pressure[5,6], which may cause re-bleeding after the evacuation of intracranial hematoma and even lead to brain hernia. High blood pressure induced by cough can also result in the risk of cerebral hemorrhage and bleeding from surgical wounds. Furthermore, cough itself may also cause severe complications such as tracheospasm and bronchospasm[7]. Also, sore throat[8] and hoarseness[9] are common adverse events after general anesthesia. Although pharyngeal pain and hoarseness are mostly mild and self-limited, they may result in strong adverse emotional experiences in patients, reduce patients' satisfaction with the surgical process, and ultimately result in a poor medical experience. To reduce the occurrence of postoperative airway-related complications, many interventions have been proposed, such as intravenous injection of fentanyl, remifentanil, dextromethopyrimidine [10], and other drugs[11], extubation under deep anesthesia[12], local application of local anesthetics[13,14], filling of lidocaine in the tracheal catheter cuff[15-17], intratracheal administration of lidocaine^[18], intravenous injection of lidocaine^[19-21] and so on. Among these, intracuff lidocaine can be used as local anesthesia, to reduce complications during extubation, and to avoid the side effects of lidocaine on the circulation and central nervous system during general application. Nevertheless, lidocaine is not easy to diffuse in the cuff, and adding sodium bicarbonate can greatly enhance the diffusion ability of lidocaine, so as to achieve better action on the tracheal mucosa[22]. Therefore, it is necessary to perform a systematic review and metaanalysis to summarize the efficacy of intracuff alkalinized lidocaine in the prevention of postoperative airway-related complications.

MATERIALS AND METHODS

We followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines for the reporting of meta-analyses of randomized controlled trials (RCTs)[23]. The protocol was registered in the International Prospective Register of Systematic Reviews (trial registration number: CRD42020178143).

Search strategy

A comprehensive literature search of PubMed (until May 2020), Embase (until May 2020), Cochrane (until May 2020), and Web of Science (until May 2020) was performed. We used a combination of free text and database-specific subjects (*i.e.*, MESH or EMTREE headings) to describe 'lidocaine'. The search strategy is shown in Supplementary material: Appendix A. No language restrictions were placed on inclusion. Non-English studies were translated using online translation. Finally, the references of all articles retrieved from the search were manually scrutinized for any relevant trials not identified using the strategy described above.

Inclusion and exclusion criteria

Studies were selected if they were: (1) Conducted as an RCT; (2) Compared intracuff alkalinized lidocaine fills with a control (*i.e.*, with air or saline fills) in patients ≥ 18 years old who received tracheal intubation under general anesthesia; and (3) Reported the incidence of cough, hoarseness, sore throat and/or visual analogue scale (VAS) of sore throat, among other outcomes. Selected studies were then excluded if they met one or more of the following criteria: (1) The trial included emergency surgery; (2) It was a small-scale preliminary pilot study; (3) The necessary data could not be extracted or calculated from the published results; (4) Other lidocaine administration methods were included in the experimental group; and (5) There were other intervention measures in the experimental group.

Outcomes

The primary outcome was the incidence of post-extubation cough. Secondary outcomes included the following: Incidence of postoperative hoarseness, the incidence of a postoperative sore throat within 24 h, VAS of a postoperative sore throat at 1 h and 24 h.

Screening and data extraction

Two independent reviewers (Chen ZX and Shi Z) screened the retrieved titles and abstracts for potential inclusion, reviewed the full text of potential studies, and extracted the data from studies that met the inclusion criteria. Any discrepancies between the reviewers were resolved through a consensus process. When the two reviewers failed to reach an agreement, the final decision was made by the third reviewer (Wang B). Data extraction was completed by two coauthors (Chen ZX and Shi Z) using a predesigned piloted data extraction form. The data extraction form collected information regarding the year of publication; primary author; country of origin; types of surgery; participant characteristics (gender, age, number, inclusion and exclusion criteria); intervention; lidocaine and placebo group events; severity of postoperative sore throat. Dichotomous data were converted to incidences for data synthesis, and continuous data were recorded using mean ± SD. Any disagreement was resolved through the consensus process discussed previously.

Assessment risk of bias

The risk of bias was assessed in duplicate using the method outlined in the Cochrane Risk of Bias Tool for Non-Randomized Studies. The risk of bias was assessed as low, moderate, high, for each selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. Any disagreement was resolved by consensus.

Statistical analysis

The meta-analysis was performed using RevMan 5.3 software (Cochrane Collaboration, Oxford, England). The level of evidence quality of each study was estimated according to the guidelines of the grading of recommendations, assessment, development, and evaluation (GRADE). We examined the following five categories: Risk of bias, consistency, directness, imprecision, and reporting bias. RCTs began as high-quality evidence and were rated down based on the described criteria. The evidence grades were classified as high quality (further research is unlikely to change the confidence in the estimate of effect), moderate quality (further research is likely to



have an important impact on our confidence in the estimate of effect and may change the estimate), low quality (further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate), or very low quality (we are very uncertain about the estimate).

If necessary, standard deviations from the confidence interval (CI) limits, the standard error, or the range values provided in the past studies were estimated. The effect sizes of dichotomous outcomes were reported as risk ratios (RR), and the mean difference (MD) was reported for continuous outcomes.

Heterogeneity was assessed using the Cochrane *Q* test and I^2 statistic. $I^2 < 50\%$ was considered low heterogeneity, $I^2 = 50\%$ to 75% as moderate, and $I^2 = 75\%$ to 100% as high. P values < 0.05 were considered statistically significant. A fixed-effect model was used if heterogeneity was considered low. If I^2 statistic $\geq 50\%$ and P < 0.05, a randomeffects model was applied to the data. The statistical methods of this study were reviewed by Peng Z from the Department of Maternal, Child, and Adolescent Health, School of Public Health, Anhui Medical University, Hefei, China.

A sensitivity analysis was performed to assess the potential influence in our analysis. We attempted to exclude RCTs with: (1) A high risk of bias; (2) Only female subjects; and (3) Cuff prefilling.

RESULTS

Study selection

A total of 580 articles were identified from the primary electronic databases (PubMed: 188, Embase: 194, Cochrane: 109, Web of Science: 89. After removing duplicates, we screened 416 studies based on the abstracts, among which 62 full-text articles were assessed for eligibility. Finally, 12 studies were included in the analysis (Figure 1).

Study characteristics/participants

The 12 included studies involved a total of 1175 participants with an average age ranging from 36.71 years to 52.00 years, and gender ratios ranging from 0-1.96. All studies were RCTs with placebo or no treatment control arms. Seven trials included patients with an ASA status of I and II[24-30]. Five trials included patients with an ASA status of I, II, and III[31-35]. The included surgeries were: One gynecological surgery[30]; two lumbar surgeries[33,34]; one orthopedic, spine and general surgery [25]; one gynecological, orthopedic, or plastic surgery[26]; one gynecological or plastic surgery[28]; one thyroidectomy surgery[29]. Four studies did not report the type of surgery[24,27,32,35]. Opioids were used in all studies except one which did not report on the use of anesthetics^[24]. Saline and air were used in the control group in three and seven experiments[24,25,28,29,33-35], respectively. Two experiments used both saline and air[27,31]. One of the experiments using air in the control group also used 1.4%NaHCO₃ as an intervention^[29]. In addition, 5 studies lubricated the cuff of the tracheal tube with sterile water or water-soluble gel or normal saline spray before intubation [26,29,30,33,34], and 2 studies performed prefilled at least 90 min before tracheal intubation[32,35] (Table 1).

Risk-of-bias and GRADE assessment

Six trials were judged to be a low risk of bias in all domains. Six trials had an unclear risk of bias, mostly related to random sequence generation and allocation concealment. Two trials had a high risk of bias. The domain that was judged to have a high risk of bias was performance bias and detection bias (Figure 2). The GRADE assessment demonstrated an overall high quality of evidence for the incidence of post-extubation cough and hoarseness. The quality of evidence for the following outcomes was considered moderate: incidence of a postoperative sore throat at 24 h, VAS of a postoperative sore throat at 1 h and 24 h (Supplementary material: Appendix B).

Incidence of post-extubation cough

The aggregate effect of the 7 studies (n = 629) evaluating the effect of intracuff alkalinized lidocaine on the incidence of post-extubation cough was in favor of lidocaine over the control (RR: 0.38; 95% CI: 0.23-0.63). Subgroup analysis revealed that the use of intracuff alkalinized lidocaine could also result in a large reduction in postextubation cough regardless of the lubricated cuff. Concerning subgroup analysis, a significant effect in the reduction of the post-extubation cough was found in the lubricated group (RR: 0.30; 95% CI: 0.13, 0.68) compared with the non-lubricated group



Table 1 Characteristics of the included trials

Trial	Country	Age (yr)	Male/ Female	Sample size	ASA status	Surgery	Intervention/comparator	Outcomes
Rizvanović <i>et al</i> [<mark>31</mark>], 2019	Bosnia and Herzegovina	49.4 (18- 65)	44/46	90	I, II, III	Elective surgery	1 Alkalinized 2% lidocaine; 2 0.9% saline; 3 Air	IPOST
Nath <i>et al</i> [<mark>32</mark>], 2018	USA	52 (18- 80)	73/127	200	I, II, III	NR	1 Alkalinized 2% lidocaine; 2 0.9% saline	IPC
Gaur <i>et al</i> [<mark>24</mark>], 2017	Arabia	44.62 (18- 65)	51/49	100	I, II	NR	1 Alkalinized 2% lidocaine; 2 Air	IPOST
Suma <i>et al</i> [<mark>25</mark>], 2015	India	37.66 (18- 65)	NR	200	I, II	Elective orthopedic, spine, and general surgery	1 Alkalinized 2% lidocaine; 2 Air	VAS of POST
Navarro <i>et</i> al[<mark>26]</mark> , 2012	Brazil	NR (≥ 18)	13/37	50	I, II	Elective gynecological, orthopedic, or plastic surgery	1 Alkalinized 4% lidocaine; 2 0.9% saline	IPC, IPH, IPOST
Shroff and Patil[<mark>27</mark>], 2009	UK	36.71 (18- 60)	51/99	150	I, II	NR	1 Alkalinized 2% lidocaine; 2 0.9% saline 3 Air	IPC, IPH
Navarro et al[<mark>28]</mark> , 2007	Brazil	45.15 (18- 65)	NR	50	I, II	Gynecological surgery or plastic surgery	1 Alkalinized 2% lidocaine; 2 Air	IPOST
Estebe <i>et al</i> [29], 2005	USA	47.67 (≥18)	13/47	60	I, II	Thyroidectomy surgery	1 Alkalinized 2% lidocaine (8.4%NaHCO ₃); 2 Alkalinized 2% lidocaine (1.4%NaHCO ₃); 3 Air	IPC, IPH, VAS of POST
Estebe <i>et al</i> [33], 2004	UK	49.67 (≥18)	39/21	60	I, II, III	Lumbar spinal surgery	1 Alkalinized 2% lidocaine (lubricated with sterile water); 2 Alkalinized 2% lidocaine (lubricated with water-soluble gel); 3 Air	IPC, IPH, VAS of POST
Estebe <i>et al</i> [<mark>34</mark>], 2002	USA	46.5 (≥18)	27/23	50	I, II, III	Lumbar spinal surgery	1 Alkalinized 2% lidocaine; 2 2% Lidocaine; 3 Air	IPC, IPH, VAS of POST
Navarro et al[<mark>35</mark>], 1997	USA	40.15 (NR)	18/88	106	I, II, III	NR	1 Alkalinized 2% Lidocaine; 2 Air	IPOST, VAS of POST
D'Aragon <i>et al</i> [30], 2013	Canada	41.8 (≥18)	0/59	59	I, II	Elective gynecological surgery	1 Alkalinized 2% lidocaine; 2 0.9% saline	IPC

IPC: Incidence of post-extubation cough; IPH: Incidence of postoperative hoarseness; POST: Postoperative sore throat; IPOST: Incidence of postoperative sore throat; VAS: Visual analogue scale; NR: Not reported.

> (RR: 0.53; 95%CI: 0.37-0.75). However, there was no subgroup difference in relation to lubrication of the cuff (P = 0.21) (Figure 3).

Incidence of postoperative hoarseness

Based on the data pooled from 5 trials (n = 370), the use of intracuff alkalinized lidocaine demonstrated a large reduction in postoperative hoarseness (RR: 0.38; 95%CI: 0.21-0.69) (Figure 4).

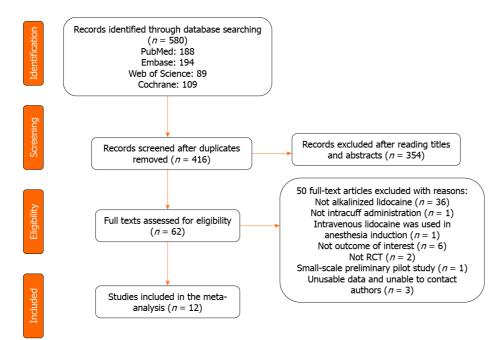
Incidence of a postoperative sore throat within 24 h

The data from four trials (n = 290) indicated that intracuff alkalinized lidocaine reduced the incidence of a postoperative sore throat within 24 h (RR: 0.19; 95% CI: 0.09-0.41) (Figure 5).

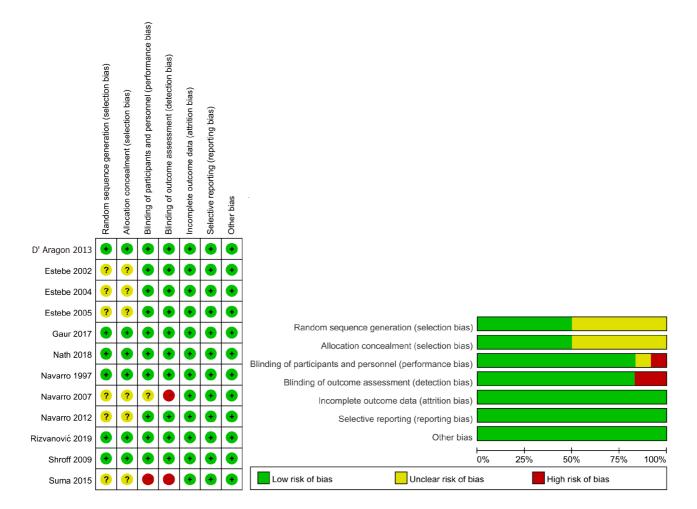
VAS of a postoperative sore throat at 1 h and 24 h

Five trials that included 476 participants demonstrated a large reduction in the VAS of a postoperative sore throat at 1 h with the use of intracuff alkalinized lidocaine (MD: -18.30; 95%CI: -22.79, -13.82) (Figure 6). Similarly, in the 5 studies (n = 476) that evaluated intracuff alkalinized lidocaine on the VAS of a postoperative sore throat at 24 h, a significant benefit of alkalinized lidocaine compared with the control was identified (MD: -14.86; 95%CI: -15.75, -13.98) (Figure 7).











Assessment of publication bias

The funnel plot for the included studies showed an asymmetrical characteristic, which suggested a possible publication bias (Figure 8).



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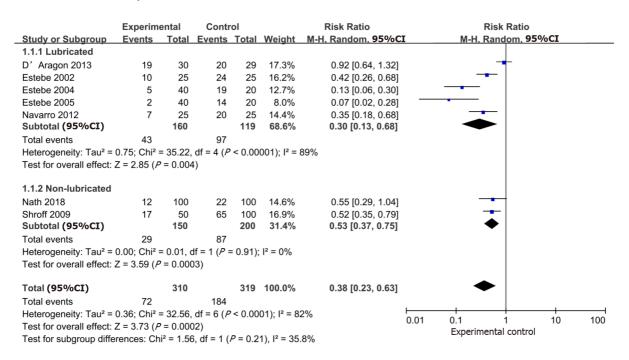


Figure 3 Forrest plots showing the effects of the intervention. Incidence of postoperative cough. CI: Confidence interval.

	Experim	ental	Contr	ol		Risk Ratio			Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95%C	I	М-Н,	Random, 9	5%CI	
Estebe 2002	1	25	19	25	7.4%	0.05 [0.01, 0.36]	<	•	·		
Estebe 2004	6	40	16	20	20.2%	0.19 [0.09, 0.40]		-	-		
Estebe 2005	12	40	15	20	24.2%	0.40 [0.23, 0.68]		_			
Navarro 2012	10	25	11	25	22.2%	0.91 [0.47, 1.75]			-		
Shroff 2009	16	50	63	100	26.0%	0.51 [0.33, 0.78]					
Total (95%CI)		180		190	100.0%	0.38 [0.21, 0.69]					
Total events	45		124								
Heterogeneity: Tau ² =	0.32; Chi ²	= 15.47,	df = 4 (<i>P</i>	= 0.00	4); l² = 749	%				10	100
Test for overall effect:	Z = 3.16 (<i>F</i>	P = 0.002	2)				0.01	0.1 Experim	ו ental control	10	100

Figure 4 Forrest plots showing the effects of the intervention. Incidence of postoperative hoarseness. CI: Confidence interval.

Experimental		Contr	ol		Risk Ratio		Risk Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95%C	I	M-H	, Fixed, 95	%CI	
Gaur 2017	4	50	20	50	53.3%	0.20 [0.07, 0.54]			-		
Navarro 2007	2	25	11	25	29.3%	0.18 [0.04, 0.74]		-			
Navarro 2012	0	25	3	25	9.3%	0.14 [0.01, 2.63]	←	•			
Rizvanović 2019	0	30	4	60	8.1%	0.22 [0.01, 3.93]		•		-	
Total (95%CI)		130		160	100.0%	0.19 [0.09, 0.41]		-	•		
Total events	6		38								
Heterogeneity: Chi ² =	0.06, df = 3	P = 1.	00); $I^2 = 0$	%			—				
Test for overall effect:	Z = 4.28 (<i>F</i>	< 0.000	01)				0.01	0.1 Experim	1 ental contro	10 I	100

Figure 5 Forrest plots showing the effects of the intervention. Incidence of a postoperative sore throat within 24 h. Cl: Confidence interval.

DISCUSSION

In this study, 12 RCTs on the prevention of postoperative airway complications with intracuff alkalinized lidocaine were included. This meta-analysis showed that intracuff alkalinized lidocaine could significantly reduce the incidence of post-extubation cough with high quality of evidence, compared with the control group, and many surgical patients may benefit from the application of intracuff alkalinized lidocaine in clinical practice. At the same time, subgroup analysis showed that saline lubrication before intubation reduced the incidence of post-extubation cough; nonetheless, the observed differences were not statistically significant. Therefore, the evidence in this study

	Experimental		Control			Mean Difference		Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95%C	I	IV, Rand	<u>om, 95%CI</u>	
Estebe 2002	3	4	25	30	13	25	21.3%	-27.00 [-32.33, -21.67]		-		
Estebe 2004	12.5	19.72	40	31	13	20	14.8%	-18.50 [-26.86, -10.14]				
Estebe 2005	15.6	8.5	40	31.4	12.3	20	19.8%	-15.80 [-21.80, -9.80]				
Navarro 1997	7.9	18.1	53	18.7	27	53	14.1%	-10.80 [-19.55, -2.05]			-	
Suma 2015	15.8	3.4	100	33	4.8	100	30.0%	-17.20 [-18.35, -16.05]				
Total (95%CI)			258			218	100.0%	-18.30 [-22.79, -13.82]		•		
Heterogeneity: Tau ² = Test for overall effect:				-	= 0.00	5); I² =	73%		⊢ -100	-50 Experimenta	l control	0 100

Figure 6 Forrest plots showing the effects of the intervention. Visual analogue scale of a postoperative sore throat at 1 h. Cl: Confidence interval; SD: Standard deviation.

	Exp	eriment	tal	С	ontrol			Mean Difference		Mean Difference	;e	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95%C	I	IV, Fixed, 95%	OCI	
Estebe 2002	1	3	25	13	9	25	5.7%	-12.00 [-15.72, -8.28]		-		
Estebe 2004	4.5	11.28	40	24	7	20	3.6%	-19.50 [-24.15, -14.85]		-		
Estebe 2005	14.7	7.2	40	28	10.1	20	3.2%	-13.30 [-18.26, -8.34]		-		
Navarro 1997	14.5	24.8	53	25.6	27.5	53	0.8%	-11.10 [-21.07, -1.13]				
Suma 2015	4.15	2.5	100	19.1	4.16	100	86.7%	-14.95 [-15.90, -14.00]				
Total (95%CI)			258			218	100.0%	-14.86 [-15.75, -13.98]		+		
Heterogeneity: Chi ² = Test for overall effect:		•			6				⊢ -100	-50 0 Experimental control	50	100

Figure 7 Forrest plots showing the effects of the intervention. Visual analogue scale of a postoperative sore throat at 24 h. Cl: Confidence interval; SD: Standard deviation.

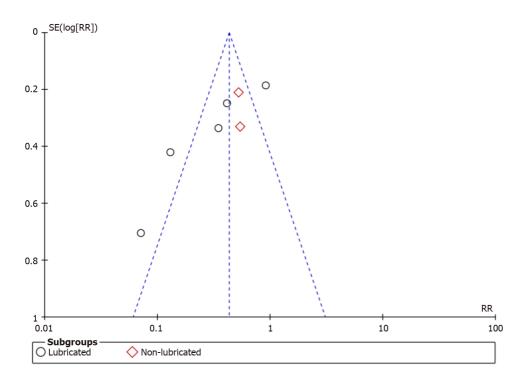


Figure 8 Funnel plot for evaluation of potential publication bias. RR: Risk ratio.

strongly suggests that intracuff alkalinized lidocaine can prevent post-extubation cough, and further study is unlikely to change this conclusion. Regarding the VAS of a postoperative sore throat at 1 h and 24 h, intracuff alkalinized lidocaine reduced the severity of postoperative sore throat at 1 h or 24 h. Similarly, the use of intracuff alkalinized lidocaine demonstrated a large reduction in postoperative hoarseness.

In terms of safety, there is no doubt that the usage of intracuff alkalinized lidocaine is much safer than the usage of intravenous lidocaine. In terms of the extubation time, no study has shown that intracuff alkalinized lidocaine may prolong the extubation

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Table 2 Sensitivity analyses: The effect of potential biases on primary and secondary outcomes													
Potential bias or limitations excluded	IPC RR (95%CI), /²	IPH RR (95%CI), P	IPOST within 24 h RR (95%CI), <i>I</i> ²	VAS of POST at 1 h RR (95%CI), <i>P</i>	VAS of POST at 24 h RR (95% Cl), <i>P</i>								
Overall	0.38 (0.23, 0.63), 82%	0.38 (0.21, 0.69), 74%	0.19 (0.09, 0.41), 0%	-18.30 (-22.79, -13.82), 73%	-14.86 (-15.75, -13.98), 43%								
Only females	0.33 (0.20, 0.52), 69%	NE	NE										
Cuff prefilling	0.35 (0.19, 0.63), 85%	NE	NE	-17.59 (-18.69, -16.49), 77%	-14.81 (-17.22, -12.41), 54%								
A high risk of bias	NE	NE	0.19 (0.08, 0.48), 0%	-18.45 (-25.61, -11.29), 77%	-14.37 (-18.31, -10.43), 56%								

IPC: Incidence of post-extubation cough; IPH: Incidence of postoperative hoarseness; POST: Postoperative sore throat; IPOST: Incidence of postoperative sore throat; VAS: Visual analogue scale; CI: Confidence interval; NE: Not estimable; RR: Relative risk.

> time. None of the trials reported any adverse events directly related to the use of intracuff alkalinized lidocaine.

> In the present study, we performed a detailed literature search, which included the main RCTs on the subject of intracuff alkalinized lidocaine. Our methodology followed strict guidelines developed by the Cochrane Collaboration. A bias risk assessment was conducted for each trial. Also, the quality of available evidence was assessed using grading criteria. The robustness of the obtained results was also tested by sensitivity analysis.

> Two previous systematic reviews and meta-analyses have also demonstrated the effectiveness of intracuff alkalinized lidocaine for the prevention of airway complications in patients with tracheal intubation; nonetheless, our study is different to these studies. First of all, previous studies did not distinguish between adult and pediatric patients, while the present study focused on adult patients. Secondly, based on the huge difference in diffusion velocity between alkalinized lidocaine and nonalkalinized lidocaine in tracheal intubation, in the present study, we only included the relevant literature on alkalinized lidocaine in the analysis. At the same time, the previous systematic review and meta-analysis were not limited, although they also carried out the corresponding subgroup analysis. Thirdly, regardless of whether lubricating the cuff before intubation may have an important impact on postoperative airway complications in patients undergoing endotracheal intubation, it is necessary to analyze lubrication of the cuff before intubation in order to eliminate the influence of confounding factors on the results. Finally, 12 RCTs were included in this study, while the previous study only included 9 RCTs[36] and 8 RCTs[37] in the alkalized lidocaine subgroup. Additional trials will provide more data and information to support the conclusions of this study.

> Our results revealed that intracuff alkalinized lidocaine decreased postoperative airway complications. To achieve a significant therapeutic effect, large doses of lidocaine may be necessary without alkalinization[37]. According to Estebe et al[34], plasma lidocaine levels confirmed the increased diffusion of lidocaine through the cuff when lidocaine was alkalinized. Moreover, this increased diffusion did not lead to vocal cord palsy. Therefore, the use of a small dose of alkalinized lidocaine (40 mg) is a relatively easy and safe practice that avoids the use of large doses of lidocaine.

> The main limitation and disadvantage of this study is the obvious heterogeneity, although a pre-defined subgroup analysis was performed. Clinically, opioids, inhalational anesthetics, and the depth of anesthesia during extubation may have an impact on cough, hoarseness, and sore throat after extubation. In order to minimize these possible confounding factors, we conducted a special sensitivity analysis. Metaanalysis still showed the effectiveness of intracuff alkalinized lidocaine when we excluded RCTs with: (1) A high risk of bias; (2) Only female subjects; (3) Cuff prefilling (Table 2). However, there are still many variables, such as operation time, inflation volume of the tracheal catheter cuff, anesthesiologist's expertise and ability, which were not systematically reported in the selected studies, thus cannot be analyzed. In addition, only 7 studies with primary outcome were eligible for inclusion, and the funnel plot results are not accurate. To sum up, the use of intracuff alkalinized lidocaine after tracheal intubation is a simple, economical and safe choice to prevent postoperative cough, sore throat, and hoarseness in adult patients. Anesthesiologists can use this technique in clinical patients.

CONCLUSION

This meta-analysis revealed that intracuff alkalinized lidocaine decreased postoperative airway complications, including coughing, hoarseness, and sore throat. Furthermore, for patients with a post-extubation sore throat, it could also reduce the degree of pain.

ARTICLE HIGHLIGHTS

Research background

Tracheal intubation is the most commonly used airway management method in general anesthesia. However, this approach has been associated with some problems, such as postoperative airway complications, which are common phenomena and adverse reactions in patients who underwent elective general anesthesia. To reduce the occurrence of postoperative airway-related complications, many interventions have been proposed. Among these, intracuff alkalinized lidocaine can be used as local anesthesia, to reduce complications during extubation, and to avoid the side effects of lidocaine on the circulation and central nervous system during general application.

Research motivation

Intracuff lidocaine can be used as local anesthesia, to reduce complications during extubation, and to avoid the side effects of lidocaine on the circulation and central nervous system during general application. Nevertheless, lidocaine is not easy to diffuse in the cuff, and adding sodium bicarbonate can greatly enhance the diffusion ability of lidocaine, to achieve better action on the tracheal mucosa.

Research objectives

Perform a systematic review and meta-analysis to summarize the efficacy of intracuff alkalinized lidocaine in the prevention of postoperative airway-related complications.

Research methods

A comprehensive literature search of Pubmed (until May 2020), Embase (until May 2020), Cochrane (until May 2020), and Web of Science (until May 2020) was performed. Heterogeneity was assessed using the Cochrane Q test and I^2 statistic. A fixed-effect model was used if heterogeneity was considered low. If l^2 statistic $\geq 50\%$ and P < 0.05, a random-effects model was applied to the data.

Research results

Twelve randomized trials (1175 patients) met the inclusion criteria. The meta-analysis showed that intracuff alkalinized lidocaine was associated with less cough compared to that produced by placebo. Similarly, intracuff alkalinized lidocaine was more effective than the control in reducing postoperative sore throat at 24 h and postoperative hoarseness. Five trials that included 476 participants demonstrated a large reduction in the visual analogue scale of a postoperative sore throat at 1 h or 24 h with the use of intracuff alkalinized lidocaine.

Research conclusions

Intracuff alkalinized lidocaine decreased postoperative airway complications, including coughing, hoarseness, and sore throat. Furthermore, for patients with a postextubation sore throat, it could also reduce the degree of pain.

Research perspectives

The use of intracuff alkalinized lidocaine after tracheal intubation is a simple, economical and safe choice to prevent postoperative cough, sore throat, and hoarseness in adult patients. Anesthesiologists can use this technique in clinical patients.

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