Appendix A – Search Strategies

Search Strategy: Pubmed

(lidocaine OR Xyloneural OR Octocaine OR Xylesthesin OR Xylocaine OR Xylocitin OR Dalcaine OR lignocaine) AND ("airway complications" OR cough OR coughing OR pharyngitis OR laryngospasm OR "laryngeal spasm" OR laryngismus OR "tracheospasm" OR "tracheal spasm" OR "tracheal spasm" OR laryngospasms OR "Laryngeal Spasm" OR "Laryngeal spasms" OR "larynx spasm" OR "sore throat" OR pharyngalgia OR hoarseness OR "airway management")

Search Strategy: EMBASE

"(('sore throat'/exp or 'sore throat' or 'coughing'/exp or 'coughing' or 'hoarseness'/exp or 'hoarseness' or 'laryngospasm'/exp or ' laryngospasm ' or 'bronchial spasm'/exp or 'bronchial spasm' or 'pharyngitis'/exp or ' pharyngitis ') and ('lidocaine'/exp or 'lidocaine')) and ('general anesthesia'/exp or 'general anesthesia')".

Search Strategy: Cochrane

- #1 MeSH descriptor: [Lidocaine] explode all trees
- #2 MeSH descriptor: [Airway Extubation] explode all trees
- #3 MeSH descriptor: [Anesthesia, Endotracheal] explode all trees
- #4 MeSH descriptor: [Intubation, Intratracheal] explode all trees
- #5 MeSH descriptor: [Airway Management] explode all trees
- #6 MeSH descriptor: [Cough] explode all trees
- #7 MeSH descriptor: [Laryngismus] explode all trees
- #8 MeSH descriptor: [Bronchial Spasm] explode all trees
- #9 MeSH descriptor:[hoarseness] explode all trees
- #10 #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9
- #11 #1 and #10

Search Strategy: Web of Science

(lidocaine OR Xyloneural OR Octocaine OR Xylesthesin OR Xylocaine OR Xylocitin OR Dalcaine OR lignocaine) AND ("airway complications" OR cough OR coughing OR pharyngitis OR extubation OR laryngospasm OR "laryngeal spasm" OR laryngismus OR "tracheospasm" OR "tracheal spasm" OR "tracheal tube" OR laryngospasm OR Laryngospasms OR "Laryngeal Spasm" OR "Laryngeal spasms" OR "larynx spasm" OR "sore throat" OR pharyngalgia OR hoarseness OR "airway management")

Appendix B—The GRADE assessment

Intracuff alkalinized lidocaine for the Prevention of	postoperative airway complications in adults
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Patient or population: Surgical patients

Settings: Perioperative setting

Intervention: Intracuff alkalinized lidocaine

Comparison: placebo

Outcomes	Assumed risk	comparative risks* (95% CI) Corresponding risk	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Control	Intracuff alkalinized lidocaine	DD 0 20	(20)		
Incidence of cough after	Study popu		RR 0.38	629	$\oplus \oplus \oplus \oplus$	
extubation	577 per	219 per 1000	(0.23 to 0.	63) (7 studies)	high	
	1000	(133 to 363)				
	Moderate					
	700 per	266 per 1000				
	1000	(161 to 441)				
Incidence of cough after	Study popu	lation	RR 0.3	279	$\oplus \oplus \oplus \oplus$	
extubation - Lubricated	815 per	245 per 1000	(0.13 to 0.	68) (5 studies)	high	
	1000	(106 to 554)				
	Moderate					

	_			
	800 per	240 per 1000		
	1000	(104 to 544)		
Incidence of cough after	Study pop	ulation	RR 0.53 350	$\oplus \oplus \oplus \oplus$
extubation - Non-lubricated	435 per	231 per 1000	(0.37 to 0.75) (2 studies)	high
	1000	(161 to 326)		
	Moderate			
	435 per	231 per 1000		
	1000	(161 to 326)		
Incidence of postoperative sore	Study pop	ulation	RR 0.19 290	$\oplus \oplus \oplus \Theta$
hroat at 24 hour	238 per	45 per 1000	(0.09 to 0.41) (4 studies)	moderate ¹
	1000	(21 to 97)		
	Moderate			
	260 per	49 per 1000		
	1000	(23 to 107)		
Incidence of postoperative	Study pop	ulation	RR 0.38 370	$\oplus \oplus \oplus \oplus$
hoarseness	653 per	248 per 1000	(0.21 to 0.69) (5 studies)	high
	1000	(137 to 450)		
	Moderate			
	750 per	285 per 1000		
	1000	(157 to 517)		
VAS of postoperative sore throat		The mean vas of postoperative sore throat at 24 hour in	476	$\oplus \oplus \oplus \Theta$
at 24 hour		the intervention groups was	(5 studies)	moderate ²
		14.86 lower		
		(15.75 to 13.98 lower)		

VAS of postoperative sore throat	The mean vas of postoperative sore throat at 1 hour in	476 • • • • •
at 1 hour	the intervention groups was	(5 studies) moderate ²
	18.3 lower	
	(22.79 to 13.82 lower)	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our 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. Very low quality: We are very uncertain about the estimate.

¹ detection bias

² performance bias

Appendix C—sensitivity analysis

Sensitivity analysis on incidence of post-extubation cough: exclude RCTs with subjects were only females

	Experim	ental	Contr	ol		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C		M-H, Random, 95% C	1	
1.1.1 Lubricated										
Estebe 2002	10	25	24	25	20.5%	0.42 [0.26, 0.68]				
Estebe 2004	5	40	19	20	14.5%	0.13 [0.06, 0.30]				
Estebe 2005	2	40	14	20	8.1%	0.07 [0.02, 0.28]		- -		
Navarro 2012	7	25	20	25	17.4%	0.35 [0.18, 0.68]				
Subtotal (95% CI)		130		90	60.5%	0.23 [0.11, 0.47]				
Total events	24		77							
Heterogeneity: Tau ² =	0.37; Chi ²	= 10.88,	df = 3 (P	= 0.01); l² = 72%					
Test for overall effect:	Z = 4.03 (F	9 < 0.000)1)							
1.1.2 Non-lubricated										
Nath 2018	12	100	22	100	17.6%	0.55 [0.29, 1.04]				
Shroff 2009	17	50	65	100	21.9%	0.52 [0.35, 0.79]				
Subtotal (95% CI)		150		200	39.5%	0.53 [0.37, 0.75]		•		
Total events	29		87							
Heterogeneity: Tau ² =	0.00; Chi ²	= 0.01, d	lf = 1 (P =	= 0.91);	l² = 0%					
Test for overall effect:	Z = 3.59 (F	9 = 0.000	03)							
Total (95% CI)		280		290	100.0%	0.33 [0.20, 0.52]		•		
Total events	53		164							
Heterogeneity: Tau ² =	0.22; Chi ²	= 15.88,	df = 5 (P	= 0.00	7); l ² = 69%	/ 0	⊢ 0.01	0.1 1	10	100
Test for overall effect:	Z = 4.65 (F	o < 0.000	001)				0.01	experimental control	10	100
Test for subgroup diffe	erences: Ch	i ² = 4.32	2, df = 1 (P = 0.0	4), l² = 76.8	3%		experimental control		

Sensitivity analysis on incidence of post-extubation cough: exclude RCTs with cuff prefilling

	Experime	ental	Contr	ol		Risk Ratio		Risk Ra	atio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C		M-H, Randor	n <u>, 95% Cl</u>	
1.1.1 Lubricated										
D'Aragon 2013	19	30	20	29	19.7%	0.92 [0.64, 1.32]				
Estebe 2002	10	25	24	25	18.7%	0.42 [0.26, 0.68]				
Estebe 2004	5	40	19	20	15.2%	0.13 [0.06, 0.30]		_ - _		
Estebe 2005	2	40	14	20	10.0%	0.07 [0.02, 0.28]				
Navarro 2012	7	25	20	25	17.0%	0.35 [0.18, 0.68]				
Subtotal (95% CI)		160		119	80.6%	0.30 [0.13, 0.68]				
Total events	43		97							
Test for overall effect: . 1.1.2 Non-lubricated Shroff 2009	17	50	., 65	100	19.4%	0.52 [0.35, 0.79]		-		
Subtotal (95% CI)		50		100	19.4%	0.52 [0.35, 0.79]		◆		
Total events Heterogeneity: Not app Test for overall effect:		= 0.002	65 2)							
Total (95% CI)		210		219	100.0%	0.35 [0.19, 0.63]		•		
Total events Heterogeneity: Tau ² = Test for overall effect: Test for subgroup diffe	Z = 3.44 (P	= 0.000)6)	< 0.00	001); l² =	85%	L 0.01	0.1 1 experimental c	l 10 ontrol	100

Sensitivity analysis on incidence of postoperative sore throat at 24h: exclude RCTs with a high risk of

bias

	Experim	ental	Contr	ol		Risk Ratio		Risk Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fix	<u>ed, 95% C</u>	1		
Gaur 2017	4	50	20	50	75.4%	0.20 [0.07, 0.54]						
Navarro 2012	0	25	3	25	13.2%	0.14 [0.01, 2.63]	←		<u> </u>			
Rizvanović 2019	0	30	4	60	11.4%	0.22 [0.01, 3.93]		•				
Total (95% CI)		105		135	100.0%	0.19 [0.08, 0.48]		\bullet				
Total events	4		27									
Heterogeneity: Chi ² =	0.05, df = 2	(P = 0.	97); l² = 0	%					1	10		
Test for overall effect:	Z = 3.56 (F	9 = 0.000	04)				0.01	0.1 experimental	control	10	100	

Sensitivity analysis on VAS of postoperative sore throat at 1h: exclude RCTs with a high risk of bias

	Experimental				ontrol			Mean Difference		Mean Di	fference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl		IV, Rando			
Estebe 2002	3	4	25	30	13	25	28.0%	-27.00 [-32.33, -21.67]		-			
Estebe 2004	12.5	19.72	40	31	13	20	22.9%	-18.50 [-26.86, -10.14]					
Estebe 2005	15.6	8.5	40	31.4	12.3	20	26.9%	-15.80 [-21.80, -9.80]					
Navarro 1997	7.9	18.1	53	18.7	27	53	22.2%	-10.80 [-19.55, -2.05]					
Total (95% CI)			158			118	100.0%	-18.45 [-25.61, -11.29]		•			
	Heterogeneity: Tau ² = 40.17; Chi ² = 12.87, df = 3 (P = 0.005); $I^2 = 77\%$ Fest for overall effect: Z = 5.05 (P < 0.00001)											50	100

Sensitivity analysis on VAS of postoperative sore throat at 1h: exclude RCTs with cuff prefilling

	Exp	erimen	tal	С	ontrol			Mean Difference		Mean D	ifference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% C		IV, Fixe	<u>d. 95% Cl</u>		
Estebe 2002	3	4	25	30	13	25	4.2%	-27.00 [-32.33, -21.67]		-			
Estebe 2004	12.5	19.72	40	31	13	20	1.7%	-18.50 [-26.86, -10.14]					
Estebe 2005	15.6	8.5	40	31.4	12.3	20	3.3%	-15.80 [-21.80, -9.80]					
Suma 2015	15.8	3.4	100	33	4.8	100	90.7%	-17.20 [-18.35, -16.05]					
Total (95% CI)			205			165	100.0%	-17.59 [-18.69, -16.49]		•			
Heterogeneity: Chi ² =	12.79, d	f = 3 (P	= 0.00	5); l² = 7	7%				⊢ -100	-50	 0	50	100
Test for overall effect:	Z = 31.4	0 (P < 0	0.00001	1)					-100	experimental	control	00	100

	Exp	Experimental Control						Mean Difference		се			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rand	<u>om, 95</u>	% CI	
Estebe 2002	1	3	25	13	9	25	33.1%	-12.00 [-15.72, -8.28]					
Estebe 2004	4.5	11.28	40	24	7	20	28.3%	-19.50 [-24.15, -14.85]		-			
Estebe 2005	14.7	7.2	40	28	10.1	20	26.9%	-13.30 [-18.26, -8.34]		-			
Navarro 1997	14.5	24.8	53	25.6	27.5	53	11.7%	-11.10 [-21.07, -1.13]			-		
Total (95% CI)			158			118	100.0%	-14.37 [-18.31, -10.43]		•			
Heterogeneity: Tau ² = Test for overall effect:					0.08); I	² = 56%	, D		-100	-50 experimental	0 contro	50 50	100

Sensitivity analysis on VAS of postoperative sore throat at 24h: exclude RCTs with a high risk of bias

Sensitivity analysis on VAS of postoperative sore throat at 24h: exclude RCTs with cuff prefilling

	Experimental Control					Mean Difference		e					
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rand	<u>om, 95%</u>	% CI	
Estebe 2002	1	3	25	13	9	25	22.4%	-12.00 [-15.72, -8.28]		+			
Estebe 2004	4.5	11.28	40	24	7	20	17.2%	-19.50 [-24.15, -14.85]		-			
Estebe 2005	14.7	7.2	40	28	10.1	20	15.8%	-13.30 [-18.26, -8.34]		-			
Suma 2015	4.15	2.5	100	19.1	4.16	100	44.7%	-14.95 [-15.90, -14.00]					
Total (95% CI)			205			165	100.0%	-14.81 [-17.22, -12.41]		•			
Heterogeneity: Tau ² = Test for overall effect:					.09); l	² = 54%	D		-100	-50 experimental	0 contro	50	100