Elective fibreoptic tracheal intubation in the operative room for anticipated difficult airway: a systematic review and meta-analysis of randomized controlled trials.

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Background Awake fibreoptic intubation (AFOI) is the recommended strategy for surgical patients with anticipated difficult airway, especially when concurrent difficult ventilation is expected.

Methods We performed the first systematic review of randomized controlled trials (RCTs) assessing different protocols for AFOI in anticipated difficult airway, including studies investigating elective AFOI for scheduled surgery; RCTs comparing different methods for performing AFOI; adult patients with anticipated difficult airway. We excluded studies in the non-operating theatre settings, RCTs comparing AFOI to other techniques, and studies based on simulation. Primary outcomes were success rate and death; secondary outcomes were major adverse events.

Results Thirty-seven RCTs evaluating 2045 patients and 4 areas were identified: premedication, local anaesthesia, sedation, ancillary techniques to facilitate AFOI. Quality of evidence was moderate-low and based on small-sampled RCTs. Overall, 12 (0.59%) intubation failures and 7 (0.34%) severe adverse events occurred, with no permanent damage or death. All evaluated methods to achieve local anaesthesia performed similarly well. No differences were observed in success rate with different sedatives. Dexmedetomidine resulted in fewer desaturation episodes compared to propofol and opioids with or without midazolam (relative risk, RR 0.51 [95% confidence interval, CI 0.28 to 0.95], p=0.03); occurrence of desaturation was similar with remifentanil versus propofol, while incidence of apnoea was lower with sevoflurane versus propofol (RR 0.43 [95% CI 0.22 to 0.81], p=0.01). A high degree of efficacy and safety was observed with minimal differences among different protocols; dexmedetomidine might offer a better safety profile compared to other sedatives.

Conclusions All the approaches resulted highly safe and effective, confirming the relevance and reliability of AFOI, although peri-procedural protocols were highly heterogeneous. Dexmedetomidine for sedation might be slightly safer to propofol and opioids with or without midazolam. Further, larger studies are required to identify the impact of procedural protocols on major clinical outcomes.

Table 1: randomized controlled trials comparing different local anaesthesia methods for elective fibreoptic tracheal intubation in the operative room for anticipated difficult airway. The thick horizontal lines separate similar comparisons.

First Author (ref)	Intervention	Comparator	N. patients intervention	N. patients comparator	Premedication	Sedation	Success rate intervention	Success rate comparator	N. reported severe adverse events intervention	N. reported severe adverse events comparator	Main findings and statistically significant differences
Wieczorek PM[13]	nebulised 2% lidocaine 40 ml	nebulised 4% lidocaine 40 ml	14	13	sodium citrate 30 ml orally, metoclopramide 10 mg, glycopyrrolate 0.3 mg and ondansetron 4 mg intravenously	midazolam and fentanyl	100%	100%	0	0	no differences between groups in haemodynamics, in time to airway topicalisation and in time for airway manipulation between the two study groups. Peak plasma lidocaine concentration was higher in the 4% group without signs of toxicity.
Woodruff C[14]	nebulised 1% lidocaine 40 ml	nebulised 2% lidocaine 40 ml	11	10	sodium citrate 30 ml orally, metoclopramide 10 mg, glycopyrrolate 0.3 mg and ondansetron 4 mg intravenously	midazolam 1-2 mg + fentanyl 100-150 µg	100%	100%	0	0	2% lidocaine group showed shorter time for intubation, better operator's satisfaction and better patients' tolerance but higher peak plasma lidocaine concentrations, without signs of toxicity. Hemodynamic response was not different.
Vasu BK[15]	nebulised 4% lidocaine 10 ml using DeVilbiss Model 163 atomiser (DeVilbiss Healthcare, Somerset, Pennsylvania, USA)	transtracheal injection lidocaine 4% lidocaine 4 m	16	17	glycopyrrolate 0.2 mg intravenously; two sprays of 10% lidocaine into each nostril and 1 ml of 2% lidocaine jelly	intravenous fentanyl 1–2 µg/kg in incremental doses	100%	100%	0	0	Trans-tracheal injection resulted in lesser patient discomfort, faster intubation and comparable haemodynamic
Kundra P[16]	nebulized 4% lidocaine 4 ml	topical anaesthesia of nasal mucosa with cotton swabs soaked with 4% lidocaine+ bilateral superior laryngeal nerve block (3 ml, 2%)+ trans-laryngeal block (2 ml, 4%) with lidocaine	24	24	diazepam (10 mg orally), morphine (0,15 mg/kg intramuscolarly), glycopyrrolate (0,2 mg intramuscolarly) and 2-3 drops of 0.05% xylometazoline in each nostril	incremental doses of 2,5 mg of diazepam intravenously	100%	100%	0	0	no difference in intubation time or end-tidal carbon dioxide level after intubation. A higher heart rate and mean arterial pressure increases were observed in the nebulized lidocaine group. No differences in nasal bleeding between the two groups.
Gupta B[17]	4% lidocaine 10 ml by ultrasonic nebulizer	blocks with 2% lidocaine of bilateral superior laryngeal nerve	25	25	oral ranitidine 150 mg , glycopyrrolate 5 µg/kg intramuscularly	midazolam 20 µg/kg + fentanyl 1 µg/kg	100%	100%	0	0	the nebulisation group showed a longer time to intubation, worse local cord opening, a higher incidence of cough and gag, a higher demand of supplemental lidocaine. No differences in haemodynamics.

		and trans-tracheal instillation of lidocaine, plus viscous xylocaine gargles twice				intravenously					
Dhasmana S[18]	2% lidocaine 10 ml by ultrasonic nebuliser	2% lidocaine 5 sprays in nasal cavity and nasopharynx, followed by 2% lidocaine with the spray-as-you-go technique (spray on the supraglottic areas, then glottic area, and finally below the cords)	30	30	intravenous glycopyrrolate 0.004 mg/kg and ondansetron 0.08 mg/kg. 0.1% xylometazoline 2 drops in each nostril	midazolam 0.05 mg/kg and fentanyl 2 µg/kg	100%	100%	0	0	no differences in haemodynamics and oxygenation. The nebulisation group was more comfortable and required less lidocaine
Xue FS[19]	2% lidocaine spray-as-you-go technique (spray on the supraglottic areas, then laryngeal area, and finally below the cords)	4% lidocaine spray-as-you-go technique (same technique)	26	26	atropine 10 µg/kg intravenously + 5 intraoral sprays of 10% lidocaine	fentanyl 1,5 µg/kg + midazolam	100%	100%	0	0	no difference in comfort score and coughing score, in total intubation time and hemodynamic. Higher total dosage of lidocaine was used in the 4% group
Malcharek MJ[20]	nebulization of 4% lidocaine 2 ml on the vocal cords and then by 2 ml of 4% lidocaine beneath the glottis by the FOB connected to the Enk Atomizer (Cook, Limerick, Ireland)	Trans-laryngeal injection of 4% lidocaine 4 ml	59	61	midazolam 3.5-7 mg 1h before surgery, orally. glycopyrrolate 0.2 mg. Five sprays of 10% lidocaine into the oral cavity followed by nebulization of 4% lidocaine	midazolam as clinically required	95% (3 failures)	100%	0	0	the trans-laryngeal technique was faster and showed less gagging and coughing, but presented more tracheal mucosal bleedings. No differences in haemodynamics, operators' satisfaction, pain, hoarseness, difficulty of swallowing or recall
Pirlich N[21]	2% lidocaine by the FOB connected to the Enk Atomizer (Cook, Limerick, Ireland), injected along all the passages from nostril to vocal cords	2% lidocaine with the spray-as-you-go technique (spray 5 ml on the laryngeal area, and then below the cords)	48	48	oral benzodiazepine; 2% lidocaine 1 ml plus 0.25% phenylephrine in each nostril; one 10% lidocaine spray was applied twice onto the oropharynx.	sufentanil bolus (< 60 kg: 5 µg; > 60 kg: 10 µg; > 100 kg: 15 µg)	98% (1 failure)	100%	0	0	patients' comfort was better using the atomiser technique, with fewer coughs or severe coughing episodes. The atomiser technique was quicker with less lidocaine administration and a lower incidence of nasal pain 4 weeks after surgery. No differences in terms gagging, grimacing or defensive movements, oxygen saturation, heart rate, blood pressure, depth of sedation or BIS
Ambi US[22]	Ultrasound guided block of internal branch of the superior laryngeal nerve with 2% lidocaine 1 ml	anatomical landmark guided block of internal branch of the superior laryngeal nerve with 2% lidocaine 1 ml	20	20	nebulisation with 3 mL 4% lidocaine over 10 min, intravenous glycopyrrolate 10 µg/kg	midazolam 0.03 mg/kg	100%	100%	0	0	Ultrasound‑guided block showed a lower incidence of coughing and gagging, a shorter time to intubation, more stable hemodynamic and better patient's tolerance

FOB: fiberoptic bronchoscopy

BIS: bispectral index

Table 2: randomized controlled trials comparing different sedation methods for elective fibreoptic tracheal intubation in the operative room for anticipated difficult airway. The thick horizontal lines separate similar comparisons.

First Author (ref)	Intervention	Comparator (and second comparator if any)	N. patients intervention	N. patients comparator *(n. patients second comparator if any)*	Premedication	Local anesthesia	Success rate intervention	Success rate comparator *(success rate second comparator)*	N. severe adverse events intervention	N. severe adverse events comparator	Main findings and statistically significant differences
Bergese SD[23]	dexmedetomidine 1mcg/kg + 0.7mcg/kg/h (rescue midazolam)	saline (rescue midazolam)	55	50	glycopyrrolate	lidocaine, any administration, including nerve blocks	100%	100%	0	0	no difference in ease of intubation, hemodynamic stability, patient cooperation and recall, but in the placebo group more patients required midazolam, fentanyl and propofol
Hassan ME[24]	dexmedetomidine 1mcg/kg	dexmedetomidine 2mcg/kg (dexmedetomidine 1mcg/kg+and fentanyl 1mcg/kg))	50	50 (50)	metoclopramide 10mg+ ranitidine 50 mg+ atropine 0.3 mg	oximetazoline + lidocaine 2%+ adrenaline + lidocaine 2%nebulizer	100%	100% (100%)	0	0 (0)	no difference in patient recall, incidence of airway obstruction and closing of vocal cords. More limb movements in the low dose Dex group
Sharma J[24]	dexmedetomidine 0.5mcg/kg	dexmedetomidine 1mcg/kg	30	30	glicopyrrolate 0.2mg+ midazolam 0.05mg/kg/ev, ondansetron 4mg, ranitidine 50 mg	lidocaine 10%puffs tongue and oropfarynx	100%	100%	0	0	patients in the high dose group more profoundly sedated, but intubation time, tolerance, vocal cords and limbs movement, and satisfaction score did not differ; no differences in haemodynamics
Tsai CJ[16]	dexmedetomidine 1mcg/kg	TCI propofol, initial target 3mcg/ml	20	20	none	cocaine 6% for nasal canals and lidocaine 10% for thongue and hypopharinx and lidocaine 2% for glottis and vocal cords	100%	100%	0	1	intubation scores and final patient satisfaction not different. The Dex group had a lower incidence of vocal cords closure and airway obstruction, better patient comfort scores, but a higher incidence of recall
Gupta K[27]	dexmedetomidine 1mcg/kg + propofol (dosage not reported)	propofol (dosage not reported)	23	23	metoclopramide 10 mg + glicopyrrolate 0.2 mg	xylometazoline + lidocaine 4% + adrenaline	100%	100%	0	0	in the Dex group, sedation was reached with less time (but the total intubation time was similar) and less propofol, the procedure was easier and better tolerated, and airway obstruction less frequent
Chalam KS[28]	dexmedetomidine 1mcg/kg + 0.5mcg/kg/h	propofol 1mg/kg	50	50	diazepam 10 mg + ranitidine 150 mg + glicopyrrolate 0.2 mg kg/ev	lidocaine 2% + adrenaline+ recurrent translaringeal nerve block with transtracheal injection 2% lidocaine	100%	100%	0	0	no difference in oxygenation during the procedure. In the Dex group heart rate, systolic and diastolic blood pressure were lower, and respiratory rate higher; in the same Dex group, patients' sedation and discomfort scores, endoscopy and intubation scores were better (but without

											differences in post intubation conditions)
Hu R[29]	dexmedetomidine 1.5mcg/kg, then 0.7 mcg/kg/h	TCI remifentanil, initial target 3 ng/m	20	20	none	ephedrine, nitrofurazone, lidocaine 7%	100%	100%	2 (bradycardia)	2 (oxygen desaturation)	no differences in intubation and post intubation scores. The Dex group had better endoscopy and patient satisfaction scores, less recall and higher oxygen saturation at the end of the procedure, but a higher incidence of cough and longer duration of procedure
Liu HH[30]	dexmedetomidine 1mcg/kg + 0.3 mcg/kg/h	remifentanil 0.75mcg/kg + 0.1 mcg/kg/min	45	45	0.1 mg phenobarbital + 0.5mg atropine	lidocaine 2% from mouth to glottis and below vocal cords	100%	100%	0	0	no difference in need of rescue propofol infusion, intubation scores, duration, hemodynamic and oxygenation. Recall more common in the remifentanil group
Shen SL[31]	dexmedetomidine 1mcg/kg/10min	TCI sufentanyl, initial target 3ng/m	20	20	none	lidocaine 2% nasal and oral and glottis	100%	100%	not reported	not reported	Dex group showed more favourable vocal cords and limbs movements, cough, patient tolerance and satisfaction scores, a shorter duration of the procedure, and a lower incidence of hypertension and respiratory depression (but a higher incidence of bradycardia)
Li CW[32]	dexmedetomidine 0.5mcg/kg+ midazolam 0.25mcg/kg/h	sufentanyl-midazolam	25	25	midazolam 0.02 mg/kg	tetracaine 1% for nostrils, + lidocaine spray as you go	100%	100%	0	0	easiness of the procedure, patient reactions, satisfaction and recall, hemodynamic and oxygenation were not different. In Dex group, sedation level was deeper, BIS index was lower and post intubation end tidal CO2 were lower
Chu KS[33]	dexmedetomidine 1mcg/kg	fentanyl 1mcg/kg	16	14	none	lidocaine 10% spray and cocaine 6%	100%	100%	0	0	no difference in blood pressure values and oxygenation. In Dex group, intubation score, patient satisfaction and amnesia were better, and heart rate was lower
Sayeed T[34]	dexmedetomidine 1mcg/kg	fentanyl 1mcg/kg + midazolam 1 mg	16	16	none	oxymetazoline 0.05% nostril, lidocaine for oropharynx and nostrils, lidocaine 2% for trachea	100%	100%	0	0	no difference in patient comfort during and after the procedure, in its length, in oxygenation, in the ease of FOB; on the contrary, the ease of intubation and diastolic blood pressure were better in the Dex group. Recall was more common with Dex.

Agrawal A[35]	dexmedetomidine 1mcg/kg + propofol (dosage not reported)	fentanyl 1mcg/kg + midazolam 1 mg	30	30	glycopyrrolate0.2mg	xylometazoline + lidocaine 4%	100%	100%	0	0	Comfort scores during FOB and intubation not different, no difference in the ease of the procedure. Respiratory rate and oxygenation higher in Dex group
Yousuf A[36]	dexmedetomidine 1mcg/kg	fentanyl 2mcg/kg + midazolam 0.02mg/kg	30	39	ranitidine 150mg + ondansetron 4 mg	spray of 10% lido + nebulization lido 2% 80mg	100%	100%	0	0	In Dex group, blood pressure and heart rate remained more stable and oxygenation at intubation was better. Sedation scores were similar, but the Dex group showed better cough score and post intubation conditions
Zhang X[37]	TCI remifentanil, initial target 3ng/ml	TCI propofol, initial target 2mcg/ml	18	18	none	intranasal lidocaine 2%	100%	94% (1 failure due to glottic closure and respiratory depression)	0	0	No difference in hemodynamic and oxygenation, and in the need to increment dosage. In the propofol group, the sedation was deeper, and the vocal cords more often closed. Patient satisfaction was similar, but recall was more common with remifentanil.
Lallo A[38]	TCI remifentanil, initial target 1,5ng/ml	TCI propofol, initial target 2,5mcg/ml	30	30	hydroxyzine 1-1.5mg/kg	lidocaine 5% and naphazoline 2%, lidocaine spray and lidocaine trough fiberscope channel	97% (1 failure due to panic)	97% (1 failure due to glottic closure and respiratory depression)	0	0	no difference in oxygenation, duration, dosage increments required and final pain score. Vocal cords opening was better in remifentanil group, but sedation was lighter and recall more common
Rai MR[39]	TCI remifentanil, initial target 3ng/ml	TCI propofol, initial target 1mcg/ml	14	10	glycopirrolate 0.2mg + midazolam (70 kg, 1 mg; 70–130 kg, 1.5 mg; .130 kg, 2 mg)	cocaine 100mg nasally, lidocaine 200mg oropharynx via atomizer + lidocaine 4% vocal cords	100%	100%	0	0	No difference in sedation scores, but endoscopy more difficult and requiring more time in the propofol group. Patient tolerance was better in the remifentanil group, but recall was more common
Machata AM[40]	remifentanil 0.75mcg/kg + 0,075mcg/kg/min	remifentanil 1.5mcg/kg + 0,15 mcg/kg/min	10	12	midazolam 0.05mg/kg + glycopyrrolate 0.2mg	lidocaine 2% and oxymetazoline for nostrils	100%	100%	0	0	no difference in hemodynamic, oxygenation and discomfort. In the high dose group, sedation was deeper, end tidal CO2 higher and recall less common
Yeganeh N[41]	TCI remifentanil, initial target 0.8ng/ml	remifentanil 0.75mcg/kg + 0,075mcg/kg/min	11	11	scopolamine 20 mg + midazolam 0.03mg/kg ev, 10' before procedure	lidocaine 10% nasal mucosa	100%	100%	0	0	no difference in hemodynamic, oxygenation, intubation conditions, duration. Recall was more common in the manual group, despite similar mean infusion rates
Puchner W[42]	remifentanil 0.1mcg/kg/min	fentanest 1.5 mcg/kg + midazolam 1-10 mg	37	37	midazolam oral 15 mg<50aa, 7.5mg>50	xilometazoline and 4% lidocaine+ lidocaine 4% supra and subglottic	100%	97% (1 failure due to intolerance)	0	0	no difference in oxygenation and ease of intubation. Duration was shorter in the remifentanil group,

											with reduced blood pressure increments and reduced patient reactivity, but recall was more common.
Pean D[43]	TCI propofol, initial target 6mcg/ml	sevoflurane 8%	38	35	none	lidocaine 5% aerosol	97% (1 failure)	90% (4 failure)	1 (hypoxemia)	1 (hypoxemia)	no difference in hemodynamic, oxygenation, technical difficulty, patient recall and patient satisfaction. In the sevoflurane group, induction and procedure duration were shorter.
Robba C[44]	TCI propofol, initial target 3,5mcg/ml	sevoflurane 8%	36	36	none	lidocaine 2% topically	100%	100%	0	0	Oxygenation, duration and intubation conditions were similar. In the propofol group apnea, hypotension and low cardiac output were more common
Schaeuble J[45]	etomidate 0.2mg/kg (+ fentanyl, dosage not reported)	propofol 2mg/kg (+ fentanyl, dosage not reported)	25	14	none	cocaine 10% nasal drops+ transcricoid injection 1/lidocaine for larynx and proximal trachea	100%	100%	0	0	no difference in oxygenation, hemodynamic, lowest BIS. The etomidate group recovered spontaneous breathing earlier.

BIS: bispectral index

Dex: dexmedetomidine

FOB: fibeoptic bronchoscopy

TCI: target controlled infusion