Original Article

Comparative evaluation of intra-cuff ropivacaine, bupivacaine, and lidocaine on emergence reactions after general anesthesia

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Abstract

Background: Emergence reactions are common after general anesthesia with tracheal intubation and can be associated with severe hemodynamic consequences. Inflating the cuff with local anesthetic instead of air has been reported to prevent these problems. However, no definitive results have been obtained for the effectiveness of this method. This study tried to come to a more reasonable conclusion by conducting more studies, and we used a variety of local anesthetics.

Materials and Methods: This study was performed on 350 patients over 18 years undergoing general anesthesia using an endotracheal tube. Patients were divided into five groups based on endotracheal tube cuff inflation with lidocaine, ropivacaine, bupivacaine, isotonic saline, and air. After removing the endotracheal tube, patients were evaluated for cough, sore throat, and hoarseness.

Results: Cough, sore throat, and hoarseness were observed in 43.7%, 27.4%, and 4.6% of cases, respectively. At all measured times, all reactions in all local anesthetic groups were weaker than in the air and saline groups. The difference between the local anesthetic groups was not significant.

Conclusion: Using local anesthetics to inflate the endotracheal cuff reduces the incidence of emergence reactions from general anesthesia.

Keywords: Cough, Hoarseness, Sore throat, Lidocaine, Ropivacaine, Bupivacaine

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Introduction

Inflation endotracheal cuff tube creates a seal that allows positive pressure ventilation and reduces the likelihood of aspiration in anesthetized patients. Cuff pressure can cause postoperative sore throat, cough, and hoarseness, common complaints after tracheal intubation[1]. The emergence of cough incidence after general anesthesia in the presence of an endotracheal tube has been estimated to range from 40% to 96%[2]. During emergence, movement of the endotracheal tube can irritate the airway mucosa and cause coughing. A cough can activate the sympathetic nervous system, leading to tachycardia, hypertension, and bleeding at the surgical site[3].

Numerous modalities have shown uncertain effectiveness in preventing or minimizing emergent reactions, and cuff inflation with a local anesthetic (LA) is one of them[4]. Lidocaine has been shown to penetrate the cuff wall of the endotracheal tube[5-7], and inflating the cuff with lidocaine solution instead of air may reduce the incidence of coughing during extubation[8]. This study was designed to investigate the effect of intra-cuff LAs on emerging reactions after general

anesthesia. We hypothesized that this method would reduce the severity and incidence of reactions after extubation. We expected their effects in the R and B groups to be longer.

Methods

This randomized clinical study was conducted on 350 American Society of Anesthesiologists (ASA) Physical Status Classification System I and II patients undergoing general anesthesia with tracheal intubation at the Imam Hossein Medical Education Center in Tehran, Iran. The study was approved by the Iranian National Committee on Ethics in Biomedical Research (Approval ID: IR.SBMU.RETECH.REC.1398.032) and approved by the Iranian Registry of Clinical Trials (IRCT ID: IRCT20120910010800N4). After obtaining informed consent from patients, all patients over 18 years who underwent limb surgery in the supine position for 1 to 3 hours were included in the study. Patients with a pre-existing sore throat, hoarseness, cough, moderate to severe illness, recent respiratory infection, history of airway hyperactivity, history of prolonged intubation, smoking and drug addiction, and potential difficulties in intubation were excluded from the study. In addition, patients with an increased risk of pulmonary aspiration, a history of laryngotracheal surgery, a body mass index (BMI)>30.0, and the need for a nasogastric tube or nasal/oral airway placement were excluded from the study. Patients who required repeat laryngoscopy before intubation and an airway opening maneuver after extubation were also excluded. Patients were randomized into five equal groups: air (group A), isotonic saline (group S), lidocaine (group L), ropivacaine (group R), and bupivacaine (group B). After establishing standard monitoring (electrocardiogram, blood pressure, capnography, and pulse oximetry), all patients received general anesthesia using the same method (intravenous midazolam 0.02 mg/kg, fentanyl two micrograms/kg as premedication, propofol 1.5 mg/kg, and atracurium 0.5 mg/kg as induction). An experienced anesthesiologist intubated all patients with a Macintosh blade and high-volume, low-pressure cuffed endotracheal tubes of appropriate size. After ensuring the proper position of the tracheal tube, the cuff was inflated with appropriate materials until a slight air leak around the cuff could be heard at a positive airway pressure of 20 cm of water with a stethoscope around the neck as described by Kumar and Hirsch[9]. Mechanical ventilation was initiated to maintain end-tidal CO2 near 30 mmHg, and propofol 0.1-0.2 mg/kg/min was used to maintain anesthesia. Nitrous oxide was not used during anesthesia. After the operation's return of normal spontaneous breathing, complete awakening, clearing of the pharyngeal secretion with low power and minimal use of suction, and withdrawal of the muscle relaxant, the endotracheal tube was removed. After extubation, all cuffs were checked, all were intact, and no case of clinical LA toxicity was recorded.

The patients were examined for cough, sore throat, hoarseness, hoarseness, and electrocardiographic changes at zero, five, ten, fifteen, and thirty minutes after the tracheal tube removal. At the same time, vital signs and ECG monitoring were recorded. The classification of respiratory reactions by severity is given in Table 1. There were no complications regards tracheal intubation or cuff inflation.

Data analysis was performed using SPSS software version 17 and expressed as mean±SD or as frequencies and proportions, as appropriate. Because of the abnormal distribution of the population (confirmed by the Kolmogorov-Smirnov test), nonparametric tests such as the chi-square and Kruskal-Wallis tests were used to analyze the data. The significance level was below 0.05 in all cases.

Results

Out of 360 cases, ten patients were excluded due to incomplete data, unexpectedly difficult intubation, operative time outside the defined range (1-3 hours), and need for airway maneuvers immediately following extubation (Figure 1). The rest (n=350) were randomly divided into five groups (n=70). There were no significant differences between the five groups concerning age, gender, Cormack-Lehane classification (Table 2), weight, height, BMI (Table 3), duration of intubation, and total opioid/muscle relaxant dose (Table 4).

Table 1: Classification of airway reactions and ECG changes.

Observation	Level	Definition
Cough	**No cough**	No cough at all
	Mild	<5
	Moderate	5-8
	Severe	>8 or decreased SPO2
Sore throat	**No sor throat**	Not at all
	Mild	Mild pain
	Moderate	Pain that worsens with swallowing
	Severe	Severe pain and difficult swallowing
Hoarseness	**No hoarseness**	No voice change
	Mild	Voice changed slightly
	Moderate	complete voice change
	Severe	difficult speaking
ECG changes	**No changes**	No change
	Mild	PAC/PVC <5/minutes
	Moderate	PAC/PVC >5/minutes or increased HR by 20%
	Severe	Sustained arrhythmias

PAC=Premature atrial contractions; PVC=premature ventricular contractions

Table 2: Demographic data.

Demographic data		Group A		Group S		Group R		Group B		Group L		P-value
		N	%	N	%	N	%	N	%	N	%	
Age (years)	**18-30**	24	6.9	30	8.6	15	4.3	30	8.6	25	7.1	0.690
	31-50	33	9.4	23	6.6	34	9.7	26	7.4	35	10.0	
	>50	13	3.7	17	4.9	21	6.0	14	4.0	10	2.9	
Gender (n)	**Male**	32	9.1	37	10.6	34	9.7	36	10.3	36	10.3	0.923
	Female	38	10.9	33	9.4	36	10.3	34	9.7	34	9.7	
Cormack-Lehane classification	**1**	37	10.6	42	12.0	42	12.0	40	11.4	36	10.3	0.869
	2	29	8.3	25	7.1	26	7.4	29	8.3	31	8.9	
	3	4	1.1	3	0.9	2	0.6	1	0.3	3	0.9	
	4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	

N= number

Table 3: Height, Weight, BMI.

	Means	SD	P-value (Kruskal-Wallis
Height	171.77	8.05	0.537
Weight	73.91	9.51	0.066
BMI	25.07	2.92	0.463

SD=Standard Deviation; BMI=Body mass index

Table 5 shows the results of using intra-cuff drugs for postoperative reactions. One hundred and fifty-three cases (43.7%) had some degree of post-extubation cough. More than 20% of the cases in the LA groups had no cough immediately after extubation, more than 20% of the patients in the A and especially the S group had a mild cough, and more than 30% of the patients in the A and S groups had a moderate to a severe cough. No one in the lidocaine (L) group had a cough. The difference between the groups was significant (P-value = 0.000), but the difference between the LA groups was not (P-value = 0.565). Cough at 10 minutes had the same results, but no moderate or severe cough was reported in LA groups. Also, no severe cough was reported in the S group. The difference between the groups was significant (P-value = 0.001) but not between the LA groups (P-value = 0.755). After 30 minutes, the A and S groups had more cases of mild cough, and only two cases in the A group reported a moderate cough. The difference between all groups was significant (P-value = 0.001) but not between LA groups (P-value = 0.816). At 6 hours, only cases of mild cough were seen. The difference between all groups was also significant (p-value = 0.023), but not between LA groups (p-value = 0.680). Results at 24 hours were the same, and no cases of moderate to severe

Table 4: Duration of intubation and use of opioid and muscle relaxant.

Variable	Group A		Group S		Group R		Group B		Group L		P-value (Kruskal-Wallis
	Means	SD	Means	SD	Means	SD	Means	SD	Means	SD	
Duration of intubation (minutes)	123.71	40.48	129.00	38.90	127.21	41.10	118.86	28.16	116.86	27.16	0.197
Atracurium (mg)	47.07	12.70	44.00	7.69	47.00	12.52	46.93	12.78	47.79	12.76	0.525
Morphine (mg)	6.63	1.79	6.13	1.60	6.54	2.04	6.74	2.10	6.60	2.09	0.444
Fentanyl (ug)	239.29	71.17	220.71	56.14	237.14	72.58	245.00	71.80	243.57	69.12	0.162

SD=Standard deviation

cough were reported in either group. Again, significant differences were between all but not LA groups (p-value = 0.017, and P-value = 0.776, respectively).

Ninety-six (27.4%) patients had a sore throat 10 minutes after extubation. The mild form of this problem was more common in the A and S groups. No cases of moderate to severe forms were reported in any LA group. The difference between the groups was also significant (P-value = 0.000). Surprisingly, more mild cases were observed in the B group, leading to significant differences between the LA groups (P-value = 0.027). Sore throat 30 minutes after extubation was more evident in groups A and S. The mild form was reported in all groups but was more common in groups A and S. No cases of moderate to severe sore throat were reported in any LA group. There were significant differences within groups (P-value = 0.000) but not between LA groups (P-value = 0.070). After 60 minutes, no case of severe sore throat was reported in any group. The mild form was more evident in the A and S groups. No case in LA groups experienced a moderate form. Again, there were significant differences within groups (P-value = 0.000) but not between LA groups (P-value = 0.807). At 24 hours, only a case of mild form was reported, and LA groups had significantly fewer sore throats (P-value = 0.000). No significant differences between LA groups (P-value = 0.816) were reported.

Hoarseness was observed in 16 patients (4.6%). Severe hoarseness was not observed at any of the time points measured. Immediately after extubation, of all cases in the LA groups, only one in the R group had mild hoarseness; hence the differences between the groups were significant (P-value = 0.002). Surprisingly, we observed more cases of hoarseness afterward. Mild hoarseness was observed in all groups, and a moderate form was seen in only 2 cases in the A group. However, the overall differences were not significant (P-value = 0.243). After 30 minutes, cases of mild hoarseness were observed in all groups. Only one moderate case was in the A group, and the overall differences were insignificant (P-value = 0.544). After 6 and 24 hours of extubation, there was only one case of mild hoarseness in the A group, and the differences between the groups were insignificant (P-value = 0.404).

We also assessed arrhythmias during post-anesthesia reactions. Mild arrhythmias, such as infrequent premature atrial and ventricular contractions, were reported more frequently in the A and S groups during extubation. However, the group's difference was insignificant (P-value = 0.233). At 10 minutes, only one case in the S group still had mild arrhythmias, and no arrhythmias were reported after that.

Discussion

Post-extubation sore throat, cough, and hoarseness are common complications after general anesthesia, with an incidence varying from 40–100%[10]. These reactions can cause serious problems, including neck hematoma after thyroidectomy[11] or carotid endarterectomy[12], wound dehiscence after laparotomy[13], intracerebral hemorrhage after intracranial surgery[14], negative pressure pulmonary edema[15], and hemodynamic shifts[16,17]. Any technique that can prevent such serious reactions while maintaining airway protection is desirable. Several methods, including intravenous lidocaine18, dexmedetomidine19, fentanyl20, and remifentanil21 have been suggested to reduce coughing during emergence with various results, all of which A

Table 5: Frequency of emergence reactions.

Extubation characteristics		Measurement times	Group A		Group S		Group R		Group B		Group L		P-value
			N	%	N	%	N	%	N	%	N	%	
Cough	**Post-extubation**	**No**	31	8.9	21	6.0	46	13.1	50	14.3	49	14.0	0.000
		Mild	22	6.3	34	9.7	15	4.3	15.1	4.6	17.9	5.4	
		Moderate	11	32.4	11	32.4	7	10.0	3	0.9	2	0.6	
		Severe	6	1.7	4	1.1	2	0.6	1	0.3	0	0.0	
	After 10 minutes	**No**	35	10.0	28	8.0	45	12.9	49	14.0	48	13.7	0.001
		Mild	31	8.9	26.7	10.3	25	7.1	21	6.0	22	6.3	
		Moderate	3	0.9	6	1.7	0	0.0	0	0.0	0	0.0	
		Severe	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0	
	After 30 minutes	**No**	43	12.3	38	10.9	54	15.4	57	16.3	56	16.0	0.001
		Mild	25	7.1	32	9.1	16	4.6	13	3.7	14	4.0	
		Moderate	2	0.6	0	0.0	0	0.0	0	0.0	0	0.0	
		Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
	After 6 hours	**No**	55	15.7	54	15.4	62	17.7	63	18.0	65	18.6	0.023
		Mild	15	4.3	16	4.6	8	2.3	7	2.0	5	1.4	
		Moderate	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
		Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
	After 24 hours	**No**	64	18.3	62	17.7	69	19.7	69	19.7	68	19.4	0.017
		Mild	6	1.7	8	2.3	1	0.3	1	0.3	2	0.6	
		Moderate	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
		Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
Sore throat	**After 10 minutes**	**No**	35	10.0	38	10.9	66	18.9	55	15.7	60	17.1	0.000
		Mild	17	4.9	24	6.9	4	1.1	15	4.3	10	2.9	
		Moderate	14	4.0	7	3.0	0	0.0	0	0.0	0	0.0	
		Severe	4	1.1	1	0.3	0	0.0	0	0.0	0	0.0	
	After 30 minutes	**No**	36	10.3	38	10.9	66	18.9	57	16.3	61	17.4	0.000
		Mild	23	6.6	28	8.0	4	1.1	13	3.7	9	2.6	
		Moderate	9	2.6	4	1.1	0	0.0	0	0.0	0	0.0	
		Severe	1	1.4	0	0.0	0	0.0	0	0.0	0	0.0	
	After 6 hours	**No**	52	14.9	44	12.6	66	18.9	64	18.3	65	18.6	0.000
		Mild	14	4.0	25	7.1	4	1.1	6	1.7	5	1.4	
		Moderate	4	1.1	1	0.3	0	0.0	0	0.0	0	0.0	
		Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
	After 24 hours	**No**	63	18.0	51	14.6	68	19.4	69	19.7	68	19.4	0.000
		Mild	7	2.0	19	5.4	2	0.6	1	0.3	2	0.6	
		Moderate	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
		Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
Hoarseness	**Post-extubation**	**No**	64	18.3	61	17.4	69	19.7	70	20.0	70	20.0	0.002
		Mild	4	1.1	8	2.3	1	0.3	0	0.0	0	0.0	
		Moderate	2	0.6	1	0.3	0	0.0	0	0.0	0	0.0	
		Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
	After 10 minutes	**No**	65	18.6	66	18.9	68	19.4	69	19.7	68	19.4	0.243
		Mild	3	0.9	4	1.1	2	0.6	1	0.3	2	0.6	
		Moderate	2	0.6	0	0.0	0	0.0	0	0.0	0	0.0	
		Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
	After 30 minutes	**No**	65	18.6	66	18.9	68	19.4	69	19.7	68	19.4	0.544
		Mild	4	1.1	4	1.1	2	0.6	1	0.3	2	0.6	
		Moderate	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0	
		Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
	After 6 hours	**No**	69	19.7	70	20.0	70	20.0	70	20.0	70	20.0	0.404
		Mild	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0	
		Moderate	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
		Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
	After 24 hours	**No**	69	19.7	70	20.0	70	20.0	70	20.0	70	20.0	0.404
		Mild	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0	

	Moderate	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	
	Severe	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	

simple method is to use LAs inside the cuff. Many authors support the favorable results[22–25], but others do not[23,26–28]. Lidocaine was used in most studies. We found only one study that used bupivacaine as an intra-cuff medication. In this study, Ghalibaf found no significant differences between lidocaine 2% and bupivacaine 0.25% in reducing the incidence of cough, bucking, and laryngospasm after extubation[29]. Only one study evaluated ropivacaine in the cuff, and no efficacy of 0.5% ropivacaine in reducing the severity or incidence of postoperative sore throat was demonstrated[30]. Given this uncertainty, this clinical study was conducted to determine the comparative effects of intra-cuff LAs in reducing the risk of post-extubation reactions.

In the present study, 153 (43.7%) had a post-extubation cough. Two meta-analyses found that both alkalinized and non-alkalinized intra-cuff lidocaine significantly reduced postoperative cough and other intubation-related complications[24,31]. However, as mentioned in the reviews above, a small number of patients enrolled and the lack of appropriate control groups may affect the conclusions based on the results. Rafiei et al. examined the effects of intracuff 2% lidocaine in 180 men and found reduced post-extubation cough better than intra-cuff dexamethasone or air. No women were included in this study[32]. Soltani and Aghadovoudi in their study demonstrated the effects of different lidocaine application methods on postoperative cough and sore throat and showed that the intracuff lidocaine group had the least frequency of postoperative coughing and sore throat as compared to other groups[33]. Estebe et al reported that alkalinization of intra-cuff lidocaine increased the diffusion rate of its neutral base across the hydrophobic structure of the cuff membrane from 1% to 65% within 6 hours. They concluded that low dose alkalinized lidocaine (40 mg) could reduce the incidence of sore throat in the postoperative period[34]. Ahmady et al used alkalinized 2% lidocaine and showed that it reduced the incidence of cough and sore throat, improved endotracheal tube tolerance, and induced smooth extubation in pediatric patients[35]. Similar results were reported in numerous studies with different lidocaine concentrations[23,24,36–38], but others[27,28,39] does not support these results. Although alkalinization has been reported to improve lidocaine penetration[6], the cuff material deteriorated over time, which may increase the risk of complications from cuff rupture[7]. To our knowledge, there was no report of lidocaine overdoses and systemic toxicity or endotracheal cuff rupture in any of these studies. In our study, we did not use alkalinized medications due to simplify the study and prevent the potential risk of tracheal damage due to cuff rupture. As previously mentioned, at all times measured, a significantly reduced cough was seen in all LA groups, but the difference between the LA groups was not significant and no LA was superior to any other in this respect.

In general, 30% to 70% of patients report a sore throat after tracheal intubation[40]. It is often the only symptom of a patient in the postoperative period. The etiology of sore throat is believed to be a mucosal erosion caused by the endotracheal tube's cuff, trauma from intubation, mucosal dehydration, and patient coughing/bucking, resulting in friction between the tracheal mucosa and tracheal tube[40]. Navarro and Baughman showed reducing effects of intra-cuff lidocaine on the severity of postoperative sore throat at one hour and both the incidence and severity at 24 hours[41]. Altintes et al. used 10% lidocaine in the endotracheal tube's cuff for the same purpose and also examined plasma lidocaine levels. They showed a lower incidence of sore throat and bucking during extubation. They hypothesized that although plasma lidocaine concentrations did not reach toxic levels, the use of higher lidocaine concentrations increased the likelihood of toxicity in the event of an accidental cuff rupture[40]. Some authors supported the above results[22,25,35,36], but Rafiei et al. and others failed to demonstrate significant effects[27,28,32]. In the present study, 96 (27.4%) patients had a sore throat. LAs helped reduce its severity at all measured time points after extubation. The only minor difference was a slight increase in mild cases in the bupivacaine group, which was higher than the other LA groups but lower than the air and saline groups.

The present study observed hoarseness in 16 cases (4.6%). As with cough and sore throat cases, there are

conflicting results on the effectiveness of intra-cuff LAs in preventing this complication[24,25,30–32,34,39,42–44]. In our study, only one case had hoarseness after extubation, which is statistically significant. In other times measured, the difference between all groups was not significant. Clinically, intra-cuff LAs had no impact on postoperative hoarseness.

A limitation of our study is that endotracheal tube cuff pressure was not assessed. Another limitation was that airway suctioning is associated with a postoperative sore throat, which was not standardized. In addition, we did not measure serum levels of LAs. Furthermore, complaints about sore throat and its severity (mild, moderate, severe) are subjective rather than objective in the case of cough.

The effects of LAs in controlling symptoms such as cough, sore throat, and hoarseness after surgery are the same and superior to air and saline groups. Although we expected more prolonged effects from bupivacaine and ropivacaine, results were similar for all LA drugs at 6 and 24 hours postoperatively. In other words, while LAs were almost equally effective in reducing the intensity and frequency of post-extubation reactions, lidocaine might be more logical given its fewer cardiac side effects[45–47].

Conclusion

For the first time, we compared three LA medications with two control groups to overcome some limitations in previous studies. The present study showed the effectiveness of intra-cuff LAs in decreasing cough reflex, sore throat, and hoarseness after anesthesia. This easy-to-use, inexpensive, and effective method can improve readiness during extubation. No cuff rupture, toxicity signs, swallowing reflex suppression, or side effects occurred during the study, confirming its safety in clinical practice. Further research is needed to evaluate the optimal dose of LAs to reduce the incidence of emergence reactions significantly. We recommend this method in clinical practice to improve conditions after extubation, especially in patients with cardiovascular disease, intracranial or intraocular hypertension, or hyperreactive pulmonary disorders.

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