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

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R É S U M É

Prérequis : L'intubation trachéale induit une altération de la muqueuse laryngée qui peut être responsable de plusieurs effets indésirables au réveil anesthésique. Les anesthésiques locaux peuvent présenter une alternative pour réduire l'incidence de ces effets indésirables.

But : Dans cette étude nous évaluons l'effet de la lidocaïne instillée sur la glotte avant l'intubation ou utilisée pour gonfler le ballonnet de la sonde d'intubation, dans la prévention des effets indésirables associés à l'intubation trachéale au moment du réveil anesthésique.

Méthodes : Quatre vingt patients proposés pour une chirurgie élective de moins de 120 minutes sous anesthésie générale ont été inclus dans cette étude randomisée, contrôlée, en double aveugle. Selon qu'ils reçoivent une instillation de la glotte par de lidocaïne à 2% ou de sérum physiologique juste avant l'intubation, et selon que le ballonnet de leurs sondes d'intubation a été gonflé par de la lidocaïne à 2% ou par du sérum physiologique, les patients ont été randomisés en quatre groupes. S-S (instillation de la glotte e gonflage du ballonnet par du sérum physiologique), S-Lido (instillation par du sérum physiologique et gonflage par de la lidocaïne), Lido-S (instillation par de la lidocaïne et gonflage par du sérum physiologique), Lido-Lido (instillation et gonflage par de la lidocaïne). Le critère de jugement principal était l'incidence de la toux avant l'extubation. Les critères de jugement secondaires étaient la sévérité des maux de gorge à H1 et H24 en postopératoire et l'incidence de la dysphonie, de la dysphagie et de la dyspnée laryngée durant les 24 premières heures en postopératoire.

Résultats : L'incidence de la toux était de 80%, 70%, 30% et 20% respectivement dans les groupes S-S, S-Lido, Lido-S and Lido-Lido. Quand elle est comparée à celle du groupe S-S, l'incidence de la toux a été significativement réduite dans les groupes Lido-S et Lido-Lido mais non dans le groupe S-Lido (p1=0.003; p2=0.0003; p3=0.7 respectivement). Les maux de gorge à H1 et H24 étaient significativement moins marqués dans les groupes Lido-S et Lido-Lido (p1=0.00002 and p2=0.01). Il n'y avait pas de différence significative entre les groupes concernant l'incidence de la dysphonie, de la dysphagie et de la dyspnée laryngée.

Conclusion : Quand elle est instillée sur la glotte avant l'intubation, la lidocaïne réduit l'incidence de la toux et la sévérité des maux de gorge pour les chirurgies qui durent moins de 120 minutes. Le gonflage du ballonnet de la sonde d'intubation par de la lidocaïne ne permettait pas de réduire ni l'incidence de la toux ni les maux de gorge.

M o t s - c l é s

Anesthésie générale, Intubation trachéale, Lidocaïne, Toux, Maux de gorge, Essai randomisé

S U M M A R Y

Background: Tracheal intubation results in an alteration of the laryngeal mucosa which can lead to undesirable effects at emergence from anaesthesia. Local anesthetics, when administered topically, may represent an interesting alternative to reduce these side effects.

Aim: In this trial, we aimed to evaluate the effect of lidocaine in preventing tracheal intubation related side effects at emergence from anaesthesia, when instilled onto the glottis before intubation or used to inflate the endotracheal tube cuff.

Methods: Eighty patients scheduled to elective surgery of less than 120 minutes under general anaesthesia were enrolled in this prospective, randomized, controlled, double blind study. As they receive instillation of 2% lidocaine or saline onto the glottis before intubation, and as they have their endotracheal tube cuff filled with 2% lidocaine or saline, the patients were randomized in four groups. S-S (Saline instillation and saline in the cuff); S-Lido (saline instillation and lidocaine in the cuff); Lido-S (lidocaine instillation and saline in the cuff); Lido-Lido (lidocaine instillation and lidocaine in the cuff). The primary outcome was the incidence of coughing before extubation. The secondary outcomes were sore throat scores at H1 and H24 postoperatively and incidence of dysphagia, dysphonia and laryngeal dyspnea during the first 24 hours.

Results: Coughing occurred in 80%, 70%, 30% and 20% of patients in S-S, S-Lido, Lido-S and Lido-Lido groups respectively. When compared to S-S group, the incidence of coughing was significantly reduced in Lido-S and Lido-Lido groups but not in S-Lido group (p1=0.003; p2=0.0003; p3=0.7 respectively). Sore throat scores at H1 and H24 were significantly lower in Lido-S and Lido-Lido groups (p1=0.00002 and p2=0.01). There was no significant difference between groups regarding the incidence of dysphagia, dysphonia and laryngeal dyspnea.

Conclusion: When instilled onto the glottis before intubation, lidocaine reduced both the incidence of coughing and the severity of postoperative sore throat in surgery of less than 120 minutes. Intracuff lidocaine was not effective to reduce neither coughing nor sore throat severity.

K e y - w o r d s

General anaesthesia, Tracheal intubation, Lidocaine, Cough, Sore throat, Randomized trial

Tracheal intubation results in an alteration of the laryngeal mucosa which can lead to undesirable effects at emergence from anaesthesia [1]. This includes coughing, sore throat, dysphagia, dysphonia and dyspnea.

Coughing at emergence from anaesthesia reflects intolerance to the endotracheal tube. It may cause many clinical side effects including tachycardia, hypertension, intracranial hypertension, increased intraocular pressure and surgical complications [2, 3]. The incidence of coughing at emergence from general anaesthesia reaches in some cases 96% [4].

Sore throat, dysphagia and dysphonia are frequent and occur in 50% of patients [5, 6]. They are generally badly experienced by the patients.

Many methods have been used to prevent the side effects of tracheal intubation at emergence from general anaesthesia. This included extubation under deep anaesthesia and opioids administration [7, 8]. This was associated with a reduction of cough occurrence at extubation but exposed to delayed recovery from anaesthesia and risk of gastric aspiration [4].

Local anesthetics, when administered topically, may represent an interesting alternative to reduce endotracheal tube associated side effects without delaying awakening [9-10].

Therefore, we conducted this trial to evaluate the effect of lidocaine in preventing tracheal intubation associated side effects when instilled onto the glottis before intubation and/or used to inflate the endotracheal tube cuff.

METHODS

Patients

Patients with ASA physical status I to III aged 18 to 80 years and scheduled to undergo elective surgery of less than 120 minutes under general anaesthesia with tracheal intubation were enrolled in this prospective, double blind, controlled, randomized trial. All patients gave their informed consent to participate in this trial. The trial took place between January and April 2013. Exclusion criteria were history hypersensitivity to local anesthetics, high risk of gastric aspiration and presumed difficult airway.

Study protocol

All patients received the same anaesthesia protocol: induction with propofol (2.5 mg/kg), remifentanil (0.5 μg/kg) and cisatracurium (0.15 mg/kg), and maintenance with continuous infusion of propofol and remifentanil and boluses of cisatracurium. Before tracheal intubation, 4 ml of 2% lidocaine or 4 ml of saline were instilled onto the glottis. After intubation, the endotracheal tube cuff was filled with 2% lidocaine or saline. Thus, the patients were randomized in 4 groups: Group S-S received saline instillation and saline in the cuff; group S-Lido received saline instillation and lidocaine in the cuff; group Lido-S received lidocaine instillation and saline in the cuff; and group Lido-Lido received lidocaine instillation and lidocaine in the cuff. Randomization was performed using Random Allocation Software 1.0 (Isfahan University of medical sciences, Isfahan, Iran). An anesthesiologist not involved in the periopeperative care and data collection, prepared one syringe of 2% lidocaine or saline for glottis instillation and another syringe of 2% lidocaine or saline for cuff inflation. The anesthesiologist who performed tracheal intubation and data collection was blinded to patients' allocation.

Cuffed endotracheal tubes used in this trial had internal diameter of 7.5 mm for men and 7 mm for women (Endotracheal Tube, Cuffed; Biçakcilar, Istanbul, Turkey). They had a barrel-shaped cuff made of a polyvinylchloride membrane. Lidocaine or saline were instilled onto the glottis with a syringe fitted with an intravenous plastic cannula during laryngoscopy before intubation.

Recovery from anaesthesia was carried in the operating room. Patients were extubated when they were responsive to simple orders.

Table 1: Demographic data.

		S-S (n=20)	S-Lido (n=20)	Lido-S (n=20)	Lido-Lido (n=20)	P
Age (years)		46 ± 9	51 ± 10	45 ± 12	53 ± 9	0.3
Sex ratio		1.2	1.8	1.2	2.3	0.7
BMI (kg/m^2)		24.1 ± 3.9	24 ± 3.3	24.3 ± 4.1 2	3.1 ± 2.5	0.4
ASA status	I	5 (25%)	8 (40%)	8 (40%)	4 (20%)	0.5
	II	6 (30%)	6 (30%)	8 (40%)	8 (40%)	
	III	9 (45%)	6 (30%)	4 (20%)	8 (40%)	

Table 2: Cormack score, intubation attempts, duration of surgery.

		S-S (n=20)	S-Lido (n=20)	Lido-S (n=20)	Lido-Lido (n=20)	P
Cormack score	I	11 (55%)	12 (60%)	10 (50%)	13 (65%)	0.8
	II	9 (45%)	8 (40%)	10 (50%)	7 (35%)	
Intubation attempts						
	1	12 (60%)	17 (85%)	16 (80%)	16 (80%)	0.3
	2	8 (40%)	3 (15%)	4 (20%)	4 (20%)	
Duration of surgery (min)		82 ± 34	80 ± 42	72 ± 32	76 ± 36	0.4

Table 3: Incidence of bucking.

	S-S (n=20)	S-Lido (n=20)	P1	Lido-S (n=20)	P2	Lido-Lido (n=20)	P3	P4
Bucking	16 (80%)	14 (70%)	0.7	6 (30%)	0.003	4 (20%)	0.0003	0.7

P1: (S-Lido vs S-S); P2: (Lido-S vs S-S); P3: (Lido-Lido vs S-S); P4: (Lido-Lido vs Lido-S).

Table 4a: Sore throat scores.

	S-S (n=20)	S-Lido (n=20)	Lido-S (n=20)	Lido-Lido (n=20)	P
H1	4.1 (±1.9)	3.2 (±1.4)	0.9 (± 1.1)	0.8 (± 1.5)	0.00002
H24	1.9 (± 1.1)	1.1 (± 1.5)	0.3 (± 0.4)	0.1 (± 0.8)	0.01

Table 4b: Sore throat scores

	S-S (n=20)	S-Lido (n=20)	P1	Lido-S (n=20)	Lido-Lido (n=20)	P2
H1	16 (80%)	14 (70%)	0.7	6 (30%)	4 (20%)	0.7

P1: (S-Lido vs S-S); P2: (Lido-Lido vs Lido-S).

Table 5: Dysphagia, dysphonia, laryngeal dyspnea.

	S-S (n=20)	S-Lido (n=20)	P1	Lido-S (n=20)	P2	Lido-Lido (n=20)	P3	P4
Dysphagia	5 (25%)	4 (20%)	0.9	1 (5%)	0.1	1 (5%)	0.1	1
Dysphonia	1 (5%)	0 (0%)	0.9	1 (5%)	1	1 (5%)	1	1
Laryngeal dyspnea	0 (0%)	0 (0%)	1	0 (0%)	1	0 (0%)	1	1

P1: (S-Lido vs S-S); P2: (Lido-S vs S-S); P3: (Lido-Lido vs S-S); P4: (Lido-Lido vs Lido-S).

Outcome measures

Occurrence of coughing during emergence from anaesthesia was the primary outcome of the study and was recorded between the end of general anesthetics administration and tracheal extubation in patients that was kept without any stimulation. For secondary outcomes, sore throat was evaluated with a verbal numeric scale from 0 to 10 (0=absence of sore throat, 10=most intense sore throat the patient could imagine) at H1 and H24 postoperatively, and occurrence of dysphagia, dysphonia or laryngeal dyspnea during the first 24 hours postoperatively, was recorded. We also noted demographic data, Cormack score, number of attempts to intubate the trachea and duration of surgery.

Statistics

Qualitative data were expressed in numbers and percentages and were compared with Fisher exact test. Quantitative data were expressed in means and standard deviations and were compared with ANOVA test. P value was considered significant if under 0.05. All statistical analyses were performed with IBM SPSS 20.0 (Armonk, NY, USA).

RESULTS

A total of eighty patients were enrolled in this study, 20 in every group. There was no significant difference regarding the demographic data between groups (Table 1). The Cormack score, number of attempts to intubate the trachea and duration of surgery were equivalent in the four groups (Table 2).

Coughing was present in 16 patients (80%) in S-S group, in 14 patients (70%) in S-Lido group, in 6 patients (30%) in Lido-S group and in 4 patients (20%) in Lido-Lido group (Table 3). When compared to S-S group, the incidence of bucking was significantly reduced in Lido-S and Lido-Lido groups but not in S-Lido group (p1=0.003; p2=0.0003; p3=0.7 respectively). There was no significant difference in bucking incidence between Lido-S and Lido-Lido groups (p4=0.7) (Table 3).

Sore throat scores at H1 postoperatively, were significantly lower in Lido-S and Lido-Lido groups (p=0.00002) (Table 4a). However, there was no significant difference between S-Lido and S-S groups (p=0.8). Finally, there was no significant difference between Lido-S and Lido-Lido groups (p=0.6) (Table 4b).

Sore throat scores at H24 postoperatively, were significantly lower in Lido-S and Lido-Lido groups (p=0.01) (Table 4a).

Twenty-five percent of patients in S-S group and 20% in S-Lido group presented dysphagia during the first 24 hours postoperatively. In Lido-S and Lido-Lido groups, the incidence of dysphagia was 5%. The difference between groups was not statistically significant (Table 5).

Dysphonia and laryngeal dyspnea incidence during the first 24 hours postoperatively, was equivalent in the four groups (Table 5).

DISCUSSION

Our study demonstrated that instillation of lidocaine onto the glottis before intubation was effective to reduce the incidence of bucking at emergence from anaesthesia in surgery of less than

120 minutes. It also reduced sore throat severity in the postoperative period. However, when used to fill the endotracheal tube cuff, lidocaine was not effective to reduce neither coughing nor sore throat severity.

Emergence from anaesthesia is associated with recovery of reflexes. Coughing causes undesirable effects that may be harmful in some patients: such as tachycardia in patients with ischemic heart diseases or increased intracranial pressure in neurosurgical patients [2, 3].

Two previous studies showed that spraying the glottis with 2% lidocaine before intubation decreased significantly the incidence of coughing at emergence from general anaesthesia for surgeries lasting less than 2 hours [9, 10]. In both studies, lidocaine was sprayed using the LTA 360 Kit®. In our study, we chose to instill lidocaine onto the glottis using a syringe fitted with a plastic cannula. This is an easy way of laryngotracheal topicalization with lidocaine always available and fast to implement. Our findings are in agreement with the results of these two previous studies.

The effect of intracuff lidocaine on the incidence of bucking is controversial. Some authors used alkalinized lidocaine and others used non-alkalinized lidocaine. Those who used alkalinized lidocaine suggested that increasing the PH of the lidocaine solution would allow its gradual diffusion through the cuff membrane [11, 12]. Estebe et al. described, in two different studies, a decrease in the incidence of coughing when alkalinized lidocaine was used to inflate the endotracheal tube cuff [12, 13]. In the other hand one recent study did not find this same effect [10].

Apart from our trial, only two other studies used non-alkalinized intracuff lidocaine [14, 15]. One showed a reduction in the incidence of post-extubation coughing [14]; the other failed to prove a correlation between the use of lidocaine to inflate the endotracheal tube cuff and the incidence of coughing at emergence from anaesthesia [15].

The discordance of these results is related to the heterogeneity of the endpoints of the aforementioned studies. Those who found a positive effect of intracuff lidocaine have all chosen post-extubation coughing as primary outcome [12-14]. However, the primary outcome in all the negative studies was coughing at emergence from anaesthesia and before extubation [10, 15]. At this point of view, when the primary outcome is the same the results of these studies are in agreement when using either intracuff alkalinized or non-alkalinized lidocaine. In our study, we used non-alkalinized lidocaine and we did not find a reduction in the incidence of coughing at emergence from anaesthesia. Our results are in agreement with those of previous studies.

Tracheal intubation causes irritation of the mucosa that is responsible for sore throat. This mucosal pain is generally badly experienced by patients in the postoperative period and can be responsible for a significant part of discomfort after general anaesthesia. The effect of laryngotracheal topicalization with lidocaine on the severity of sore throat after intubation had been demonstrated in several studies [9, 10]. Our findings are in concordance with those studies. The use of intracuff lidocaine had been described to reduce the severity of sore throat [10-13, 16]. We did not find similar results in our study. The previous studies that found this positive effect had used alkalinized lidocaine while non-alkalinized lidocaine was used in the present study. This could explain the discordance. Diffusion of lidocaine through the membrane of the endotracheal tube cuff would be slower and less important when it is not alkalinized.

In our study, we also evaluated the effect of the association of laryngotracheal topicalization with lidocaine and intracuff lidocaine on the incidence of coughing and sore throat at emergence from general anaesthesia. Adding intracuff lidocaine did not potentiate the effect of lidocaine instilled onto the glottis neither in reducing the incidence of coughing nor in reducing the severity of postoperative sore throat. This is in agreement with the results of a recent trial [10].

In conclusion, 2% lidocaine instilled onto the glottis before intubation was effective to reduce both the incidence of coughing at emergence from general anaesthesia and the severity of postoperative sore throat in surgery of less than 120 minutes. Intracuff lidocaine was not effective to produce this same effect and did not potentiate the effect of laryngotracheal topicalization with lidocaine.

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