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ORIGINAL RESEARCH ANESTHESIOLOGY

Efficacy of intra-cuff alkalinized lidocaine compared to low dose lidocaine infusion in reducing extubation induced emergence phenomena

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Abstract

Background & objectives: The commonest method to secure airway in general anesthesia is with the use of endotracheal tube **(**ETT). However, ETT-induced airway and circulatory reflexes also complicate the emergence, which may lead to potentially harmful complications. We aimed to assess the efficacy of intra-cuff alkalinized lidocaine (ICAL) compared to inj. lidocaine injected intravenously (IV) in minimizing the ETT induced emergence phenomena during recovery and extubation.

Methodology: 60 patients who were candidate for elective intermediate duration operations and were in ASA class 1 and 2 were enrolled in the study. Patients were randomly assigned either to receive ICAL (mixture of 1:1 of lidocaine 2% and 1.4% NaHCO3) or 2% lidocaine 1mg/ kg IV. During recovery from anesthesia and extubation, the frequency of coughing was recorded. The patients were also monitored for development of sore throat, hoarseness of voice, laryngeal spasm and pharyngeal pain during the emergence process, and the vital signs were monitored. The data of the study were analyzed using the SPSS software 20. Statistical comparisons were done by means of independent t-test. The correlation was done between all parameters using chi-square test. Logistic regression was used to calculate odds ratio (ORs) and 95% confidence interval (CI). $p \leq 0.05$ was considered as statistically significant.

Results: ICAL is more potent in preventing cough ($p = 0.005$), severity of coughing ($p = 0.047$) and also in preventing sore throat ($p = 0.014$) compared to inj. lidocaine injected IV. There were no other side effects noted. ICAL is associated with better maintenance of both MAP and HR ($p = 0.004$ and 0.055 respectively). Although both groups showed increase in sympathetic stimulation.

Conclusions: The efficacy of intra-cuff alkalinized lidocaine is significantly higher than IV lidocaine in suppressing cough, severity of cough, sympathetic stimulation and sore throat in patient undergoing surgeries of one to two hours duration.

Key words: Intra-cuff lidocaine; Intravenous lidocaine; Emergence coughing; Endotracheal tube

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1. Introduction

Tracheal extubation and anesthesia may lead to emergence phenomena which cause airway and circulatory reflexes including hypertension, tachycardia, bronchospasm, laryngospasm, coughing, sore throat, hoarseness of voice and bucking.[1] It has been reported clinically that respiratory complications following tracheal extubation were three times more frequent than that after tracheal intubation during induction of anesthesia (12.6% vs. 4.6%).[2] There are many factors that may influence this high incidence and include cuff-trachea contact area (i.e., tracheitis), in addition to the utilization of lidocaine ointment and the endotracheal tube size (i.e., laryngitis), and the use of succinylcholine (i.e., pharyngitis). The incidence of sore throat may also be related to intra-cuff pressures. Laryngeal edema that may cause only transient hoarseness in an adult, can lead to a remarkable reduction in the laryngeal cross-sectional area in small children and may cause acute respiratory obstruction.[3]

Laryngospasm occurs with the superior laryngeal nerve stimulation, when the vocal cords spontaneously close and remain closed. This may be the result of light anesthesia, irritating gas in the airway, or mechanical irritation by the tube or secretions falling onto the vocal cords.[1]

During extubation, coughing and bucking are common. Bucking is physiologically similar to the Valsalva maneuver. When lung volume become smaller than the vital capacity, a negative pressure pulmonary edema can be the result. They often induce sudden spikes in pressures of cavities such as intracranial, intrathoracic, intraocular, and intraabdominal pressures, putting the patient at risk.[4] All these changes are accompanied by sympathetic stimulation which can lead to increase cardiac oxygen demand, bleeding and arrhythmias.[5]

Pharmacological measures including short duration narcotics,[6] dexmedetomidine,[7] and lidocaine application either topically or by intra-cuff rout, all have been used.[6,8] Every technique has its own drawbacks and lidocaine, IV or intra-cuff, has been shown to be a reliable technique.

Alkalinization of intra-cuff lidocaine has been thought to increase diffusion from the cuff multiple times as well as potentiating its action on tracheal mucosa by increasing the free part which allow us to use low dose of lidocaine and stay away of approaching toxic doses.[9]

On a bases of the previously mentioned researches we chose to utilize alkalinized lidocaine in a low dose to inflate the ETT cuff and compare it to IV lidocaine to attenuate emergence phenomena.

2. Methodology

2.1. Study design and setting:

It was a randomized, double-blind, prospective clinical trial that was conducted in the operating room complex of Madenat Al-Imamen Al-Khadumain Medical Centre, Baghdad, Iraq, from October 10, 2014 to January 15, 2015.

2.2. Ethical considerations

Approval were obtained from Iraqi Commission for Medical Specializations as well as signed informed written consent by all the patients.

2.3. Inclusion & Exclusion criteria:

Patients undergoing elective operation of 1–2 h duration, in which intubation was required, ASA class I and II, age 18-55 y, weighing between 50 and 100 kg were included in the study.

Patients with allergy to medications used in the study, or those with cough, or asthma or chronic obstructive airway disease, recent respiratory infection, active reflux in gastrointestinal system or hernia in a hiatal were excluded.

Anticipated nasogastric tube insertion after surgery, anticipated difficult intubation or failure to intubate from first time, or the patient refusal were absolute contraindications for inclusion in the study.

Anesthetic protocol:

Anesthetic induction and maintenance were same for all the patients. They were randomly allocated to either IV lidocaine group or ICAL group. Induction was done with propofol 2-2.5 mg/kg, fentanyl 1 µg/kg, paracetamol 1 g infusion during surgery and vecuronium 100 µg/kg for intubation. Anesthesia was maintained with isoflurane 0.8-1 mac in oxygen and nitrous oxide. Vecuronium was used 0 µg/kg PRN. IV fluids were used as per requirement.

Anesthesia was reversed with neostigmine 2.5 mg with atropine 1 mg.

Study procedure:

Before induction of anesthesia name, age, gender, patient identification number, weight, ASA class, name of operation and initial vital signs all were recorded.

Anesthesia was induced with medications mentioned above, then direct laryngoscopy was used to acheive endotracheal intubation using a high-volume, low-pressure cuffed ETT.

For the IV lidocaine group, the cuff was inflated with normal saline, and in the ICAL group, it was done with 2% alkalinized lidocaine mixed with 1.4% sodium bicarbonate in 1:1 volume ratio, directly prepared before administration. Audible leak test was used to determine the initial minimum occlusive pressure and it was checked on different times during operation. Isoflurane (0.8-1 MAC) was used for maintenance of anesthesia. Both groups received paracetamol 1g IV to ensure analgesia.

As we only have sodium bicarbonate of 8.4 percent the dilution was 1.6 ml of it diluted to 10 ml with normal saline then adding to it 10 ml of lidocaine 2% in this way we will have 1:1 volume, we prepared 20 ml because tubes from size 7 to 9 all may take up to this volume.

The blinded technique was ensured by preparing the medication by a colleague, who prepared the 20 ml syringes containing either normal saline or alkalinized lidocaine and 5 ml syringes of either normal saline or lidocaine 2%.

Five minutes before extubation 2% lidocaine 1 mg/kg or normal saline were administrated intravenously. Atropine and neostigmine were used at the end of surgery to reverse the neuromuscular blockade. After skin closure, isoflurane was turned off. Oral suctioning was done before extubation.

During the emergence phase, the patients were intermittently checked for recovery either verbally or with gentle tactile stimulation while receiving 100% oxygen. If the patients meet the standardized extubation requirements, they were extubated.

Table 1: Comparative demographic data and duration of surgery

Variables	Intra cuff lidocaine	IV Lidocaine	p–value
Age (y)	39.2 ± 11.3	40.1 ± 12.5	0.768
Gender [n (%)]	16 (50)	16 (50)	1
Weight (kg)	81.9 ± 11.1	83.4 ± 11.4	0.610
Duration of surgery (min)	91.2 ± 21.1	90.3 ± 21.7	0.879

Data given as Mean ± SD, unless specified.

Table 2: Comparative extubation related complications

Variables	Intra cuff lidocaine	IV Lidocaine	OR (95% CI)	P - value
Cough	4(13.8%)	14(48.3%)	5.8(1.6,21)	0.005
Coughing grade				0.047
Single cough spo_2 ≤ 95%	2(6.9%)	4(13.8%)		
More than one episode < 5 sec	1(3.4%)	5(17.2%)		
Sustained bouts > 5sec	1(3.4%)	5(17.2%)		
Sore throat	3(10.3%)	11(37.9%)	5.2 (1.2,21.7)	0.014

Data given as n (%)

Once isoflurane was discontinued, a blinded observer recorded heart rate (HR), mean arterial blood pressure (MAP), spontaneous respiratory rate (RR) and the saturation of oxygen immediately after extubation as well as the duration of the operation. The frequency of coughing episodes and their severity were recorded.

All patients were evaluated for the presence of sore throat, hoarseness of voice, laryngeal spasm and pharyngeal pain in the post anesthesia recovery unit for 30 min.

Data analysis:

The data of the study were analyzed using the SPSS software 20. Numeric variables were expressed as mean ± SD and all statistical comparisons were made by means of independent t-test with $p \leq 0.05$ considered as statistically significant. Categorical variables were expressed as numbers and analyzed by cross tabulation to assess the frequency and percentage of each variable among studied groups. The correlation was done between all parameters using chi-square based measure of association to indicate the significance of the association ($p \leq 0.05$ considered statistically significant). Logistic regression was used to calculate odds ratio (ORs) and 95% confidence interval (CI).

Repeated measure general linear method was used to measure the relationship of blood pressure and pulse rate with the route of administration of lidocaine over time. A $p < 0.05$ was considered significant.

3. Results

This study included 60 patients, 30 in each group. Two patients were excluded from the study, one in ICAL

Table 3: Comparative hemodynamic parameters in the groups. Data given as Mean ± SD

Variables	Intra cuff lidocaine	IV Lidocaine	p-value*	p-value **
Initial Mean Arterial Blood Pressure	95.03 ± 12.14	101.83 ± 7.70	0.001	0.004
Post–extubation Mean Arterial Blood Pressure	97.03 ± 11.44	105.69 ± 8.73		
Initial Heart Rate	82.90 ± 13.15	86.21 ± 6.85	0.004	0.055
Post–extubation Heart Rate	85.28 ± 11.17	92.03 ± 12.12		

** p-value over time*

*** p-value for difference between two treatment group*

group because the patient had neck trauma before the operation and the other one in IV group because the anesthetist used remifentanil which was not included in our protocol. Thus, 58 patients were analyzed, 29 in each group. Patient characteristics (age, gender and weight) between the two treatment groups showed non-significant differences (p = 0.768, 1 and 0.610 respectively) as seen in Table 1.

The duration of the operation in the two groups was statistically equivalent (p = 0.879), probably due to a narrow range of patient selection criteria (Table 1).

Results illustrated in Table 2 reveal a significant decrease in the cough incidence in patients administered an intra cuff lidocaine (5.8 times) in comparison with those who received lidocaine intravenously, 4 (13.8%) vs. 14 (48.3%) respectively (P = 0.005) as shown in Table 2.

Table 2 also shows that the severity of the cough was significantly reduced in patients receiving intra cuff lidocaine as compared to patients receiving lidocaine intravenously (p = 0.047). Incidence of Grade 1 cough was 2 (6.9%) in ICAL group as compared to 4 (13.8%) in IV group, similarly Grade 2 cough 1 (3.4%) to 5 (17.2%) and Grade 3 1 (3.4%) to 5 (17.2%) as seen in Table 2.

Significant number of the patients in our study experienced sore throat in immediate post-operative period (14 out of 58). The frequency of sore throat was also reduced significantly in patients receiving intra cuff lidocaine when compared with those receiving lidocaine via intravenous rout [3 (10.3%) vs. 11 (37.9%) p = 0.014] as illustrated in Table 2.

Additionally, results demonstrated in Table 3 reveal that patients receiving intra cuff lidocaine showed lower initial and post extubation mean arterial blood pressure than patients receiving lidocaine intravenously.

MAP and HR increased over time in both studied groups significantly (p = 0.001); but ICAL was more effective in reducing sympathetic stimulation than IV lidocaine (p = 0.004) which is very significant (Table 3).

There was zero incidence regarding other side effects; hoarseness of voice, laryngeal spasm and pharyngeal pain.

4. Discussion

In general, there was an increase in the sympathetic stimulation in both groups at the time of extubation judging from the comparison of MAP and HR at the start of operation and at the time of extubation. However, the ICAL group was associated with less sympathetic stimulation as compared to IV group.

Many clinical trials have been conducted to study various pharmacological methods to attenuate the respiratory and sympathetic reflexes in the emergence phase of anesthesia and find out the better ones. A meta-analysis by Tanaka Y et al.[10] included 1232 patients from 5 studies showing the effectiveness of both topical and IV lidocaine in attenuating ETT induced emergence phenomena compared to the placebo group and proved that the topical lidocaine was better than the IV use. Lozano et al.[11] enrolled 80 patients; data for 78 were entered into analysis. They observed that cough was present in about 65% (13 patients) in controls, 26.3% (5 patients) in the group receiving topical lidocaine, 15.8% (3 patients) in group receiving intra-cuff lidocaine, and 16.2% (4 patients) in those received lidocaine intravenously with significant difference (p < 0.05), showing that both intravenous and intra-cuff lidocaine provide the best outcome.

Earlier studied used plain lidocaine intracuff, which raise the concern of lidocaine toxicity but Huang CJ et al.[12] showed effectiveness of alkalinization and warming of lidocaine in attenuating ETT induced emergence phenomena compared to 2% and 4% lidocaine alone and placebo.

More recent research conducted by Navarro and his co-workers revealed that smokers who received alkalinized lidocaine 2% via intra-cuff, experienced a low frequency of sore throat and emergence coughing.[13] The mean dose of lidocaine used in this research was 138 ± 52 mg. In contrast to this, Wetzel and his colleagues reported that using ICL didn't cause a reduction in emergence coughing in patients subjected to surgery lasting for less than 30 min,[14] that is why we chose operations more than one hour in our study.

George et al.[15] showed that plasma level of lidocaine when given IV 1 mg/kg five min before extubation approaches desirable level to attenuate ETT induced EF unlike lidocaine instilled 10 min before extubation.

It's unclear why some patients were still coughing in our study. There may be many reasons for this, including the use of low doses of lidocaine for the two groups. In the current research, mean doses of lidocaine were around 80 mg in IV group and 40 mg in ICAL group. It is well known that the quantity of the drug that diffuses through the wall of the cuff is correlated directly to the dose of lidocaine used. Hence, using higher lidocaine concentrations could suppress the cough more effectively. As mentioned in the introduction, the main mechanism for emergence coughing is the respiratory mucosa irritation caused by ETT and its cuff, and ICAL primarily functions by removing this reflex. In the vast majority of circumstances, this explains ICAL's success. Since ICAL only anesthetizes the small region which is in a contact with the cuff, any stimulation that occur along the tracheobronchial tree (for example, oropharyngeal irritation with secretions) will also cause cough. Finally, ICAL's circumferential numbing effect

may not be uniform. Owing to gravity, air collection in the cuff, and other causes, diffusion can be greater on the posterior portion of the trachea (assuming the patient is supine). Unequal diffusion could be the cause of certain patients' uneven numbness and inability to suppress coughing.

5. Limitations

There have been some limitations;
1. Though the observer was the same in all cases but the intubating anesthetists varied in different cases, which can cause a bias.
2. We didn't have the facility to measure the plasma level of lidocaine, by which we could have been more precise in recommending specific doses or prolonged time of administration.
3. There was no control group to compare with.
4. We could not monitor the patients for 24 h postoperatively due to logistic reasons.

6. Conclusion

Intra-cuff alkalinized lidocaine is significantly more effective than intravenous lidocaine in suppressing cough and sore throat during extubation in patients undergoing surgeries between one to two hours. The intra-cuff alkalinized lidocaine reduces the cough severity and the sympathetic stimulation, more effectively than IV lidocaine during extubation.

7. Conflict of interests

None declared by the author.

8. Authors' contribution

GIK: Concept, conduction of the study work and manuscript editing

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