

The effect of intracuff alkalinized lidocaine and dexamethasone on post-extubation morbidities in smoker patients undergoing laparoscopic surgery: A double blind randomized control study[†]

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ABSTRACT

Endotracheal intubation is associated with post-operative cough, hoarseness and sore throat. Smoking inclines patients to perioperative morbidities. The aim of the study was to compare between the effect of the combination of alkalinized 2% lidocaine and dexamethasone (LD), alkalinized 2% lidocaine alone (L), dexamethasone alone (D), and air (A) on decreasing post-extubation morbidities (cough, sore throat and hoarseness), when inflated in the endotracheal tube cuff in patients who were undergoing laparoscopic surgery under general anesthesia. The main objective was to study the favorable effects of these combinations compared to air, to reduce post-extubation morbidities. A prospective, randomized, controlled, double-blind study was used. One-hundred smoking patients who underwent laparoscopic surgery participated in the study. Participants were randomly allocated to receive intra-cuff endotracheal tube agents; either alkalinized 2% lidocaine (L group, n=25), dexamethasone (D group, n=25), alkalinized 2% lidocaine + dexamethasone (LD group, n=25), or air (control group) (A group, n=25). Morbidities were evaluated at emergence, 2 hours, 8 hours and 24 hours after surgery. All 100 patients completed the study. The groups were comparable in terms of patient characteristics, anesthetic, and surgical data. The incidence of cough at 24 hours' post-surgery in group A (n=3 (12%)) was significantly higher than in group L (n=0 (0%)) (p = 0.037), group D (n=0 (0%)) (p = 0.037) and group LD (n=0 (0%)) (p = 0.037). Moreover, the incidence of sore throat at 24 hours' post-surgery in group A (n=8 (32%)) was significantly higher than group L (n=0 (0%)) (p <0.000), group D (n=0 (0%)) (p =0.000) and group LD (n=0 (0%)) (p =0.000). Furthermore, incidence of hoarseness at 24 hours' post-surgery in group A (n=10 (40%)) was significantly higher than group L (n=0 (0%)) (p = 0.001), group D (n=0 (0%)) (p=0.001) and group LD (n=1 (4%)) (p = 0.001). The instillation of the combination of alkalinized lidocaine and dexamethasone or lidocaine alone in the endotracheal tube cuff was superior to dexamethasone alone or the control group in reducing the incidence and the severity of post-extubation morbidities, which are cough, sore throat and hoarseness.

Keywords: Smoking; Lidocaine; Dexamethasone; Cough; Hoarseness; Sore throat.

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INTRODUCTION

Endotracheal intubation is generally used to keep the airway open and to ensure ventilation of the patient where general anesthesia is applied for the operation. It accelerates positive pressure ventilation and provides respiratory protection for aspiration of the stomach contents. On the other

hand, endotracheal intubated patients are more prone to intubation-related adverse events including postoperative cough, nervousness, hoarseness, and sore throat. The latter, though considered a minor complication, often interferes with the patient and remains as an unpleasant postoperative memory [1].

Among the side effects associated with the use of a cuffed endotracheal tube (ETT) is local irritation and inflammation of the airways caused by prolonged inflation of the cuff which results in post-intubation morbidity [2]. A sore throat is reported in 30% - 70% of patients after endotracheal intubation. As a cuffed ETT, the potential airway irritation and the inflammation associated with its use can be minimized by regulating the cuff pressure, and providing drugs prophylactically to reduce postoperative morbidities [3].

Cough in the development of standard anesthesia in the operating room and after anesthesia care is a serious complication with 15% -94% of patients developing a cough post-intubation, which can lead to serious problems such as increased blood pressure, myocardial infarction, cardiac arrhythmia, bronchospasm, surgical bleeding and increased intracranial pressure and eye pressure [4]. Smokers develop inflammation of the laryngeal epithelium and distortion of the tissues, which can affect laryngeal purity and function [5]. Many studies have been conducted to investigate modalities to minimize post-intubation morbidities, such as the use of high volumes of low-pressure endotracheal tubes [6], using smaller endotracheal tubes [7], inhalation of steroids [8], intravenous lidocaine and topical lidocaine [9] as a cough control [10], and filling the ETT cuff with lidocaine as a drug delivery system [2]. When lidocaine is injected into the ETT cuff [11], it spreads through the semipermeable membrane wall and induces anesthesia in the trachea and increases tolerance to tracheal tubes and their cuffs resulting in significant decrease in the incidence of post-extubation morbidities [12]. Buffering of lidocaine with bicarbonate has a high degree of diffusion through a cuff membrane, resulting in less irritation to the mucosa and less accidental damage to the cuff. It is prepared by 2% lidocaine mixed with 8.4% sodium bicarbonate, in a 19:1 mL proportion [13]. Dexamethasone is used as a topical drug to reduce sore throat after

surgery and its effect have been demonstrated in many studies [14-16].

Corticosteroids are known for their anti-inflammatory actions. By reducing or inhibiting the inflammatory response, it should be possible to reduce the incidence of postoperative cough, restlessness, hoarseness and sore throat. Studies using a topically-applied steroid, intravenous dexamethasone and inhaled fluticasone propionate have shown beneficial results in decreasing postoperative sore throat [17-20]. However, none of these methods, when used alone, completely reduced sore throat and suppressed cough post extubation.

The aim of this study was to compare the effect of the combination of alkalized 2% lidocaine plus dexamethasone, alkalized 2% lidocaine alone, dexamethasone alone and air in reducing post-extubation morbidities when inflated in the ETT cuff under general anesthesia in smokers undergoing laparoscopic surgery. The main objective was to study the favorable effects of these combinations compared to air in reducing post-extubation morbidities.

METHODS

Design

A prospective, randomized, double-blind, controlled study was used. One hundred smokers, male 23/100 (23%) and female 77/100(77%), scheduled for laparoscopic surgery under general anesthesia, aged 18-60 years with an American Society of Anesthesiologists (ASA) Classification of I or II and a Mallampati score of 1-2 were recruited to the study. All patients were smokers for longer than five years and consumed at least five cigarettes a day and did not discontinue the habit prior to the surgical procedure. Patients with significant medical history such as bronchial asthma, pharyngitis, laryngitis and upper respiratory tract infection, chronic obstructive pulmonary disease (COPD), or drug allergies were excluded from the study. Patients who required more than one attempt at intubation were excluded from the study. Patients who completely met the in-

clusion criteria were informed in the surgical department by one of the researchers about the trial's aims, methods, its risks and potential benefits before agreeing to participate. Patients knew that they would be randomly assigned to different treatments before agreeing. Informed consent was taken from the participants who agreed to participate

Sample and sampling

A formula (i.e. Pocock's sample size formula) that can be directly applied for comparison of proportions P_1 and P_2 in two equally sized groups:

$$n = \frac{[P_1(1-P_1) + P_2(1-P_2)] (Z_{\alpha/2} + Z_{\beta})^2}{(P_1 - P_2)^2}$$

Where, n: required sample size, P_1 : estimated proportion of study outcome in the exposed group (i.e. combination therapy) ($P_1 = 0.30$), P_2 : estimated proportion of study outcome in the unexposed group (control therapy) ($P_2 = 0.70$), α : level of statistical significance, $Z_{\alpha/2}$: Represents the desired level of statistical significance (typically 1.96 for $\alpha = 0.05$), and Z_{β} : Represents the desired power (typically 0.84 for 80% power).

According to the analysis, 21 patients were recommended in each group. However, 25 patients were recruited to account for the possibility of dropout. Consecutively, all patients who met the inclusion criteria were randomly divided into four groups.

Randomization

Randomization was done through opaque and well-sealed envelopes. The sequence generation was performed by using Random Allocation Software v.1.0. A number was written on each envelope and the group was written on the card within it, along with the serial number. When patients arrived, the envelope was opened to disclose the group to be allotted.

Blindness

The patients, health care providers, and the people who collected and ana-

lyzed data were unaware of the treatment group allocation.

Preparation of drugs

The agents were arranged in two syringes of 2 ml and 10 ml for each group that were similar in every respect. The syringes by various means were prepared by a separate anesthesiologist who did not participate in the study and were covered with paper wrap. The anesthesia provider was blind to the type of drug administration, as all solutions were colorless in a volume of 2 ml and 10 ml. The anesthesiologist who interacted with the participants did not participate in the patients' care after surgery.

Group (A)

Each of the two syringes were filled with air, the ETT cuff was first filled with the 2 ml syringe, and then completed with the 10 ml syringe until ETT cuff pressure became 25 ± 5 cmH₂O.

Group (D)

A 2 ml syringe was filled with 8 mg dexamethasone and a 10 ml syringe filled with distilled water. The ETT cuff was inflated with 2 ml dexamethasone and completed with distilled water until ETT cuff pressure became 25 ± 5 cmH₂O.

Group (L)

Each of the 2 ml and 10 ml syringes were filled with alkalized 2% lidocaine in the ratio of 10 ml 2% lidocaine to 0.52 ml 8.4% sodium bicarbonate. The ETT cuff was then inflated with the 2 ml syringe and completed with the 10 ml syringe until ETT cuff pressure became 25 ± 5 cmH₂O.

Group (LD)

Each 2 ml syringe was filled with 8 mg of dexamethasone and the 10 ml syringe with alkalized 2% lidocaine. The ETT cuff was inflated with the 2 ml dexamethasone and completed with alkalized 2% lidocaine until ETT cuff pressure became 25 ± 5 cmH₂O.

Procedure

This prospective study was conducted at the Department of Anesthesiology at a hospital in the North West Bank, Palestine. The study was approved by the Institutional Review Board (IRB) from An-Najah National University. Informed consent was obtained from each patient. One hundred patients scheduled for elective laparoscopic surgery were included in this prospective, randomized double-blind study. Inclusion criteria were patients between 18-60 years, of either sex, with ASA physical status I or II, and their Mallampatti classification equal to 1-2. All patients were smokers for longer than five years and consumed at least five cigarettes a day and did not discontinue the habit prior to the surgical procedure. Patients with laryngeal disease or asthma were excluded from the study. Patients with expected severe intubation, more than one attempt at intubation, and/or a history of respiratory infection were also excluded from the study. Data was collected for every participant: age, height, weight, gender, smoking, blood pressure, heart rate, respiratory rate, electrocardiogram (ECG) rhythm, peripheral capillary oxygen saturation (SpO₂), and body mass index (BMI). Ringer lactate 20 ml/kg was given 30 minutes before anesthesia induction for all patients.

All patients received a standardized anesthetic consisting of 100% pre-oxygenation. General anesthesia (GA) was introduced with Fentanyl (2 µg/kg) and Propofol (2 mg/kg). Atracurium was given (0.5 mg/kg) to ease intubation of the trachea. The mechanical ventilation was performed to keep the end tidal of carbon dioxide (ETCO₂) between 35 and 40 mmHg. After the induction of anesthesia, the laryngoscopy was executed at once using either a Macintosh 3 or 4 laryngoscope blade after which intubation ensued. The ETT cuff was filled with the solution directly after ETT inclusion and the cuff volume was adapted to maintain an airway pressure of 25 cmH₂O.

Intubation of the trachea was implemented employing a tracheal tube (Murphy™ high volume, low pressure, and polyvinylchloride (PVC) cuff) with a 7.0-7.5 mm inner diameter for females and an 8.0-8.5 mm inner diameter for males. Lubrication of ETT was done with water-soluble gel. ETT cuffs were amplified conferring to the randomized obligation of the experiment. ETT cuffs were inflated at the smallest occlusive volume (i.e. no escape was identified under controlled ventilation). We ensured, by auscultation under controlled ventilation, that there was no leak. If the cuff pressure decreased during surgery, additional air or drug could be injected into the cuff. The cuff pressure was measured by a manometer to make sure that the pressure did not exceed 25 cmH₂O. Maintenance of anesthesia consisted of air / O₂ (50% / 50%), and isoflurane MAC=1-1.2% to manage anesthesia until surgical termination (time T₀). At the end of the surgery, Atropine was given in a dose of 0.01 mg/kg and Neostigmine (0.05 mg/kg IV) for the departure of muscle relaxation. Mechanical ventilation was continued until the commencement of spontaneous respiration. When all airway criteria were fulfilled after extubation (spontaneous ventilation, ability to follow verbal commands, eye-opening or hand grip and ability to indicate appropriate movements), extubation of the trachea was done directly after Pharynx suction. The patients were then given 6L oxygen via face mask and transferred into the Post Anaesthetic Care Unit (PACU). A nurse who was unaware of the patient's group assignment evaluated sore throat, cough, and hoarseness. Hemodynamic parameters and postoperative nausea and vomiting were also documented at 2 hours, 8 hours and 24 hours in both PACU and the surgical ward. Verbal rating scales were used for the four groups of patients to assess the presence and severity of sore throat, cough, and hoarseness by an independent anesthesiologist who was blinded to patient groups when the patient was in the operating room and by nurses working in both the PACU and the surgical ward. All nurses working

in the PACU and surgical department were trained by one of the authors (IZ) on how to use the assessment tools for cough, sore throat and hoarseness before the study was conducted.

Assessment tool

Sore throat and cough were evaluated as per the patient's subjective evaluation and were graded as 0, 1, 2, and 3; where, 0: No sore throat/cough at any time since the operation, 1: Minimal sore throat/cough, 2: Moderate sore throat/cough, and 3: Severe sore throat/cough.

Hoarseness was evaluated as per the patient's subjective evaluation as follows: 0: No evidence of hoarseness at any time since the operation, 1: No evidence of hoarseness at the time of the interview, 2: Hoarseness at the time of the interview noted by the patient only, and 3: Hoarseness that is easily noted at the time of the interview.

Statistical analysis

Frequencies and percentages were used to describe demographic variables. Chi-Square tests and Fishers Exact test were used to test the differences between the four study groups for qualitative or categorical variables, and Pairwise Post-Hoc tests were then done. Means and standard deviations with One Way ANOVA tests were derived to study the differences between the four study groups regarding the quantitative, or scale, variables with LCD Post-Hoc Pairwise test. SPSS Version 20

was utilized for data analysis. A p-value of less than 0.05 was considered significant.

Ethical Considerations

The study was operated in conformance with the Helsinki Declaration and was endorsed by the IRB at An-Najah National University and the Ministry of Health of Palestine. Each potential subject was sufficiently informed by one of the authors (IZ) preoperatively when the patient was in the surgical ward of the aims and methods of the study. They were informed that the study included participants being randomized for various treatments that would be inflated in the endotracheal cuff to reduce postoperative morbidities such as cough, sore throat and hoarseness. The participants were also informed of the institutional affiliation of the researchers, the expected benefits and potential risks of the study, the nature and extent of the research question, the methodological tools that would be used to collect data and all other relevant aspects of the study. Having ensured that the potential participant had understood the information, the author then sought the freely given informed consent from the participants. It was made clear to the participants that participation was voluntary and could be terminated at any time without any penalty.

RESULTS

All 100 sampled patients completed the study. The groups were comparable in regards to patient demographic and surgical data (Tables 1 & 2).

Table (1): Demographic data of the patients in the four groups of study. Data are shown as F(ANOVA) test with Mean \pm Standard Deviations and Chi -Square test with Percentages and Frequencies*

Variable	(A) n=25 Mean \pm S.D	(L) n=25 Mean \pm S.D	(D) n=25 Mean \pm S.D	(LD) n=25 Mean \pm S.D	F Or Chi-Square	p-Value
Age (year)	46.56 \pm 13.93	45.04 \pm 13.14	44.56 \pm 12.31	44.08 \pm 13.6	0.164	0.920
Gender						
Male n (%)	3 (12%)	7 (28%)	7 (28%)	6 (24%)	2.428	0.488
Female n (%)	22 (88%)	18 (72%)	18 (72%)	19 (76%)		
BMI	26.32 \pm 3.05	25.3 \pm 3.38	25.94 \pm 3.54	27.0 \pm 2.14	1.35	0.263
Cigarettes per day (n)	11.48 \pm 9.63	12.4 \pm 10.22	10.6 \pm 7.26	13.08 \pm 9.84	0.337	0.798
Years of smoking (n)	19.28 \pm 11.58	18.72 \pm 11.96	16.56 \pm 11.55	18.44 \pm 11.24	0.337	0.798

* Chi Square test with Frequencies and Percentages used for gender; the differences were not significant between the groups.

Table (2): Anesthetic and surgical data of the patients in the four groups of study. Data displayed as F(ANOVA) test with Mean \pm Standard Deviations and Chi -Square test with Percentages and Frequencies*

Variable	Air (n=25) Mean \pm S.D	Lidocaine (n=25) Mean \pm S.D	Dexamethasone (n=25) Mean \pm S.D	Lidocaine & Dexamethasone (n=25) Mean \pm S.D	Chi-Square Or F	P-Value
ASA						
II n (%)	25 (100%)	25 (100%)	25 (100%)	25 (100%)	0.000	1.000
Mallampati score						
1 n (%)	17 (68%)	15 (60%)	17 (68%)	22 (88%)	5.197	0.158
2 n (%)	8 (32%)	10 (40%)	8 (32%)	3 (12%)		
Total Propofol (mg)	188 \pm 43.97	184.4 \pm 50.17	211.6 \pm 53.9	200.4 \pm 20.51	1.977	0.123
Total Fentanyl (μ g)	200 \pm 40.82	208 \pm 40	204 \pm 47.7	204 \pm 53.85	0.126	0.944
Total Atracurium (mg)	50.8 \pm 14.19	50.4 \pm 11.36	51.8 \pm 9.01	52.4 \pm 18.77	0.111	0.953
Total Midazolm (mg)	2.56 \pm 0.77	2.48 \pm 0.51	2.52 \pm 0.51	2.56 \pm 0.51	0.107	0.956
Duration of anesthesia time (min)	70 \pm 16.46	73.4 \pm 14.77	76.16 \pm 15.98	77.8 \pm 21.41	0.970	0.410
Duration of surgical time (min)	60.48 \pm 14.82	62 \pm 21.7	66.4 \pm 20.69	65.4 \pm 19.94	0.514	0.674
Time from first spontaneous breathing until extubation (min)	4.88 \pm 2.39	10.12 \pm 3.35	6 \pm 2.66	9.08 \pm 4.01	15.377	0.000

* Chi -Square test with Frequencies and Percentages used for Mallampati score and American Society of Anesthesiologists (ASA).

Table (3) shows that there were no statistically significant differences between the four study groups regarding hemodynamic parameters ($p > 0.05$). There were no statisti-

cally significant differences regarding the percentage of patients with post-operative nausea and vomiting (PONV) between study groups in the PACU ($p = 0.053$).

Table (3): Hemodynamic parameters of the patients in the four groups of study. Data displayed as F (ANOVA) test with Mean \pm Standard Deviations.

	A Air (n=25) Mean \pm S.D	L Lidocaine (n=25) Mean \pm S.D	D Dexamethasone (n=25) Mean \pm S.D	LD Lidocaine & Dexamethasone (n=25) Mean \pm S.D	F	p-Value
MAP during OP	87.76 \pm 10.58	88.32 \pm 14.91	85.01 \pm 6.83	88.11 \pm 10.75	0.480	0.697
MAP during emergence phase	102.85 \pm 11.39	103.06 \pm 20.11	101.82 \pm 16.94	97.53 \pm 13.29	0.667	0.575
MAP in PACU	96.25 \pm 12.29	96.96 \pm 14.37	97.42 \pm 15.22	95.12 \pm 14.1	0.127	0.944
HR during OP	79.43 \pm 9.73	75.17 \pm 9.76	80.22 \pm 10.16	79.59 \pm 9.56	1.389	0.251
HR during emergence phase	90.05 \pm 13.46	85.86 \pm 13.21	93.32 \pm 21.95	84.41 \pm 11.53	1.695	0.173
RR during emergence	20.25 \pm 7.91	18.33 \pm 6.3	15.87 \pm 4.83	16.89 \pm 7.07	2.063	0.110

Mean Arterial Pressure (MAP), Heart Rate (HR), Respiratory Rate (RR)

COUGH

Cough at emergence

There were statistically significant differences between the study groups according to the incidence of cough directly after extubation ($p < 0.001$) (Table 4). The results of pairwise comparisons showed that the incidence of cough at emergence in group A (12 (48%)) was significantly higher than group L

(3 (12%)) ($p = 0.004$), group D (1 (4%)), ($p < 0.001$) and group LD (0 (0%)) ($p < 0.001$). The results indicated that the incidence of cough at emergence was significantly lower in groups LD, L and D compared to group A. The results also showed that the incidence of cough in group L (3 (12%)) was significantly higher than in group LD (0 (0%)) ($p = 0.037$).

Table (4): Incidence and severity of cough, sore throat and hoarseness; data are expressed as number (percentage). Chi-square test was used.

	A group		L group		D group		L + D		P-values	
	Incidence	Severity	Incidence	Severity	Incidence	Severity	Incidence	Severity	Incidence	Severity
Cough										
At extubation	12 (48%)		3 (12%)		1 (4%)		0 (0%)		0.000	
PACU	7 (28%)		2 (8%)		1 (4%)		0 (0%)		0.009	
2 hr.	22 (88%)	Moderate 11 (44%)	10 (40%)	0 (0%)	4 (16%)	0 (0%)	8 (32%)	1 (4%)	0.000	0.000
8 hr.	21 (84%)	Mild 18 (72%)	1 (4%)	1 (4%)	1 (4%)	1 (4%)	0 (0%)	0 (0%)	0.000	0.000
24 hr.	3 (12%)	Mild 3 (12%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.057	0.057
Sore throat										
2 hr.	18 (72%)	Moderate 14 (56%)	2 (8%)	0 (0%)	14 (56%)	5 (20%)	5 (20%)	0 (0%)	0.000	0.000
8 hr.	18 (72%)	Mild 17 (68%)	0 (0%)	0 (0%)	10 (40%)	10 (40%)	1 (4%)	1 (4%)	0.000	0.000
24 hr.	8 (32%)	Mild 8 (32%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.000	0.000
Hoarseness										
2 hr.	21 (84%)	Noted By patient 11 (44%) Easily noted 10 (40%)	13 (52%)	12 (48%) 1 (4%) 1 (4%)	8 (32%)	4 (16%) 4 (16%)	9 (36%)	4 (16%) 5 (20%)	0.001	0.015 0.015
8 hr.	21 (84%)	Noted By patient 15 (60%) 6 (24%)	6 (24%)	6 (24%) 0 (0%)	9 (36%)	9 (36%) 0 (0%)	7 (28%)	6 (24%) 1 (4%)	0.000	0.033 0.003
24 hr.	10 (40%)	Noted by patient 10 (40%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)	1 (4%)	0.000	0.000

Post Anesthetic Care Unit (PACU)

Cough in the Post-Anesthesia Care Unit (PACU): There were statistically significant differences between the study groups in regards to the incidence of cough in the PACU ($p = 0.009$) (Table 4). The results of pairwise comparisons showed that the incidence of cough in the PACU in group A (7 (28%)) was significantly higher than group D (1 (4%)), $p = 0.015$ and group LD (0 (0%)) ($p < 0.001$).

Cough at 2 hours

There were statistically significant differences between the study groups in regards to the existence of a cough at 2 hours' post-op ($p < 0.001$) (Table 4). The results of pairwise comparisons showed that the incidence of a cough in group A (22 (88%)) was significantly higher than group L (10 (40%)), ($p < 0.001$), group D (4 (16%)) ($p < 0.001$) and group LD (8 (32%)) ($p < 0.001$). The percentage of patients with a moderate cough in group L (0 (0%)), in group D (0 (0%)) and in the LD group (1(4%)) were significantly lower than the percentage of patients in group A ($p < 0.001$) (Table 4). A significant increase in the severity of cough at moderate levels in the air group compared with the other three groups at 2 hours' post-op was noted.

Cough at 8 hours

There were statistically significant differences between the study groups in regards to the incidence of cough at 8 hours' post-surgery ($p < 0.001$) (Table 4). The results of pairwise comparisons showed that the incidence of cough in group A (21 (84%)) was significantly higher than group L (1 (4%)) ($p < 0.001$), group D (1(4%)) ($p < 0.001$) and group LD (0 (0%)) ($p < 0.001$), so all groups were superior to group A in reducing cough at 8 hours post-op. There were also statistically significant differences between the study groups according to the severity of cough at 8 hrs (for mild cough). The percentages of patients with a mild cough at 8 hours' post-op in the L group (1 (4%)), D group (1 (4%)) and

LD group (0 (0%)) were significantly lower than that of the A group (18 (72%)) ($p < 0.001$) (Table 4).

Cough at 24 hours

There were no statistically significant differences between the study groups according to incidence of cough at 24 hours ($p=0.057$) (Table 4). The results of pairwise comparisons showed that the incidence of cough in group A (3 (12%)) was significantly higher than group L (0 (0%)) ($p = 0.037$), group D (0 (0%)) ($p = 0.037$) and group LD (0 (0%)) ($p = 0.037$), so all groups were significantly superior to group A in reducing cough at 24 hours post-op.

SORE THROAT

Sore throat at 2 hours

There were statistically significant differences between the study groups according to the incidence of sore throat at 2 hours ($p = 0.009$) (Table 4). The results of pairwise comparisons showed that the incidence of sore throat in group A (18 (72%)) was significantly higher than group L (2 (8%)), $p = 0.001$ and group LD (5 (20%)) ($p < 0.001$). The results indicated that group L and group LD were superior to the other two groups (D & A) in reducing soreness of the throat at 2 hrs. There was also a significant difference in the number (and percentage) of patients with severity of sore throat at a moderate level at 2 hrs in group L (0(0%)), group D (5(20%)) and group LD (0(0%)), when compared to group A (14(56%)) ($p < 0.001$) (Table 4). The results showed a significant increase in severity of sore throat in group A compared with the other three groups at 2 hours post-op.

Sore throat at 8 hours

There were statistically significant differences between the study groups in the incidence of a sore throat at 8 hours' post-op ($p < 0.001$) (Table 4). The results of pairwise comparisons showed that the incidence of a sore throat in group A (18 (72%)) was significantly higher than group

L (0 (0%)) ($p < 0.001$) and group LD (1 (4%)) ($p < 0.001$). Also, the results showed that the incidence of a sore throat in group D (10 (40%)) was significantly higher than group L (0 (0%)) ($p < 0.001$) and group LD (1 (4%)) ($p < 0.001$), so groups L and LD were superior to the other two groups (D & A) in reducing the incidence of sore throat at 8 hours post-op. The results also showed that the number (percentage) of patients with mild soreness of throat at 8 hours was significantly higher in group A (17(68%)) compared to group L (0 (0%)), group LD (1 (4%)) and group D (10(40%)) ($p < 0.001$) (Table 4). The number (percentage) of patients with a mild sore throat at 8 hours' post-op was significantly higher in the D group (10 (40%)) compared to the L group (0 (0%)) and the LD group (1 (4%)) ($p < 0.001$). The results indicated that L and LD groups were superior to D and A groups in reducing the severity of sore throat.

Sore throat at 24 hours

There were statistically significant differences between the study groups according to the incidence of a sore throat at 24 hours' post-op ($p < 0.001$) (Table 4). The results of pairwise comparisons showed that the incidence of a sore throat in group A (8(32%)) was significantly higher than group L (0(0%)) ($p < 0.001$), group D (0(0%)) ($p < 0.001$) and group LD (0(0%)) ($p < 0.001$), so all groups were found to equally reduce sore throat at 24 hrs. compared to group A. The number of patients with a mild sore throat was significantly higher in group A compared to the other three groups ($p < 0.001$) (Table 4).

HOARSENESS

Hoarseness at 2 hours

There were statistically significant differences between the study groups regarding hoarseness at 2 hours' post-op ($p < 0.001$) (Table 4). The results of pairwise comparisons showed that the incidence of hoarseness at 2 hours in group A (21(84%)) was significantly higher than group L (13(52%)) ($p = 0.014$), group D (8(32%)) ($p < 0.001$) and group LD (9(36%)) ($p < 0.001$). Thus, all groups were superior to group A in reducing hoarseness 2 hours post-op. There were also statistically significant differences between the study groups at 2 hours' post-op regarding hoarseness (noted only by the patient) ($p = 0.015$). Hoarseness noted only by patients in the A group (11(44%)) was found in significantly higher proportions than group D (4 (16%)) and group LD (4 (16%)) ($p = 0.0325$) (Table 4). Also, there were significant differences between the L group (12 (48%)) and both the D group (4 (16%)) and the LD group (4 (16%)) ($p = 0.0164$) (Table 4). Therefore, the D group and the LD group were superior to the other two groups (A and L) in reducing hoarseness noted only by patients 2 hours' post-op (Table 4). The incidence of hoarseness (easily noted by nurse and patient) was 10 (40%) in group A, which was significantly higher than the L group (1 (4%)) ($p = 0.0024$), the D group (4(16%)) ($p = 0.0614$) and the LD group (5 (20%)) ($p = 0.015$) (Table 4).

Hoarseness at 8 hours

There were statistically significant differences between the study groups regarding the incidence of hoarseness 8 hours' post-op ($p < 0.001$) (Table 4). The results of pairwise comparisons showed that the incidence of hoarseness in group A (21 (84%)) was significantly higher than group L (6 (24%)) ($p = 0.009$) and group LD (7 (28%)) ($p = 0.009$). Thus, the L and LD groups were superior to A and D groups in reducing hoarseness 8 hours post-op. The results of the Chi-Square test showed that there were statistically significant differences between the study groups in terms of the patient's hoarseness (noted by the patient only) at 8 hours ($p = 0.033$) (Table 4). The results indicated that all three groups were significantly superior to the A group in reducing the severity of hoarseness.

Hoarseness at 24 hours

There were statistically significant differences between the study groups in the

incidence of hoarseness 24 hours' post-op ($p < 0.001$) (Table 4). The results of pairwise comparisons showed that the incidence of hoarseness at 24 hrs in group A (10 (40%)) was significantly higher than group L (0 (0%)) ($p < 0.001$), group D (0 (0%)) ($p < 0.001$) and group LD (1 (4%)) ($p < 0.001$), so all groups were superior to group A in reducing the incidence of hoarseness at 24 hrs. There were also significant differences in the severity of hoarseness at 24 hrs (noted by the patient only) between group L (0 (0%)), group D (0 (0%)) and group LD (1 (4%)) compared to the A group (10 (40%)) ($p < 0.001$). The results indicated that all groups were superior to group A in reducing the severity of hoarseness that was noted by patients at 24 hours' post-surgery (Table 4).

DISCUSSION

The main findings of the present study show that ETT intra-cuff inflation with lidocaine, with dexamethasone and with a combination of the two decreases the incidence and severity of cough, sore throat and hoarseness at different time intervals during the postoperative period in smokers undergoing laparoscopic cholecystectomy compared to patients that received ETT intra-cuff inflation with air. The results also indicate that the proportion of patients with cough on emergence from surgery was significantly lower in the LD group compared to the L group. L and LD groups were superior to the other two groups (D & A) in reducing the incidence and severity of sore throat 8 hours post-op. The D group and the LD group were superior to the other two groups (A and L) in reducing hoarseness noted only by patients at 2 hours post-op.

The results of the current study are in accordance with Jiménez-Rodríguez et al. [21] and Estebe et al. [13] whose studies showed that intra-cuff alkalized lidocaine and saline significantly diminished the incidence of airway-related side effects in comparison with air. Estebe et al. concluded that inflating the ETT cuffs with fluids removes air pockets in the ETT cuffs and

provides extra support by impeding extra intra-cuff pressure [13].

Additionally, in a study conducted by Navarro et al. [22], the authors evaluated whether ETT intra-cuff alkalized lidocaine was superior to saline in the onset of post-operative sore throat and hoarseness. The study showed that intra-cuff alkalized 2% lidocaine was superior to saline in reducing the incidence of cough and sore throat during the postoperative period in smokers. These results are consistent with the results of the current study that lidocaine reduced the incidence of cough and sore throat.

In the current study, no documentation of cuff damage was noted. The dose handled in the current study (1 ml 8.4% bicarbonate in 20 ml solution) was adequate to increment the pH of the lidocaine solution and simplify its diffusion, but was not high enough to risk injuring the trachea if any cuff damage were to have occurred. This result is consistent with study results realized by Ali et al. [23], which showed that the amount of lidocaine used was not to exceed 5 mg / kg to protect the patient from local anesthetic toxicity if the cuff were broken.

Ayoub et al. [17] showed that topical application of Betamethasone over the ETT reduced the incidence of cough, hoarseness and sore throat postoperatively, which is consistent with our study, which rather inflated the ETT cuff with dexamethasone. Park et al. [19] administered intravenous dexamethasone with double lumen intubation and found a decrease in incidence and severity of sore throat and hoarseness after extubation. Tazeh-kand et al. [20] found that inhaled fluticasone propionate given prior to induction reduced the incidence and severity of postoperative cough, sore throat and hoarseness. Steroids with their anti-inflammatory effect have been attributed to these results [19-20]. In a study by Kee et al. [24], the authors speculated that it may be possible for dexamethasone to diffuse through the ETT cuff, which interacts with tracheal mucosa in contact with it, reducing the inflammatory process

that occurs in the tracheal mucosa. Alkalized lidocaine can diffuse through the ETT cuff to tracheal mucosa, reducing the repulsion of their irritating receptors [20]. These mechanisms are likely to be responsible for the observed decrease in the incidence of cough, hoarseness and sore throat in the postoperative period.

Incidence and severity of cough

In the current study, the results indicate that the incidence of cough at emergence from general anesthesia was significantly lower in groups LD, D and L than in group A. These results are consistent with a study by Navarro et al. [22], which showed that the incidence of cough at the time of emergence from general anesthesia was significantly lower in the L group ($p=0.001$), when compared to the saline group, which shows an advantageous effect of the alkalized lidocaine by suppressing the irritation stimuli of the ETT cuff on tracheal mucosa as compared to the ETT cuff inflated with saline. The results from the current study are not in accordance with a study conducted by Choubsaz et al. [25] that showed there was no significant difference in the existence of cough after anesthesia between the control group (air) and lidocaine group. A significant increase in the severity of cough at moderate levels in the air group compared to the other three groups at 2 and 8 hours was observed in our study. These results are compatible with Ahmady et al. [26] who reported a reduction of severe cough in the lidocaine group when compared to the saline group ($p = 0.014$) in the PACU and at extubation time. Rafiei et al. [14] and Cho et al. [27] reported that dexamethasone had superiority over lidocaine in reducing the severity of cough, which was not noted in our results.

Incidence and severity of sore throat

In this study, statistically significant differences were found between the study groups regarding the incidence of a sore throat at 2 and 24 hours, $p = 0.001$. The results also show a significant increase in the severity of the sore throat in the control

group compared to the other three groups. The results of this study are consistent with the results of Huang et al. that showed that the frequency of developing a sore throat was significantly lower than the control group when lidocaine 4% and alkalized lidocaine were administered. They proposed using alkalized lidocaine as primed in the ETT cuff for serene emergence from standard anesthesia [28]. Controversially, the results of the current study are not in line with another study conducted by Porter et al. [29] in which lidocaine, air and normal saline were compared. This study found no statistical significance between the groups. Regarding the severity of sore throat, Ahmady et al. [30] found a reduction in severity of soreness of the throat in the lidocaine group compared to the saline group ($p = 0.031$) in the PACU and Ali et al. [23] reported a reduction in the severity of sore throats in the lidocaine group in comparison with air and distilled water groups.

Incidence and severity of hoarseness

Incidence of hoarseness over the course of the first 24 hours' post-operation was significantly less in the three groups compared to the A group in this study. These results are congruent with a study by Navarro et al. [22], which showed that the incidence of hoarseness at the period of release from the PACU was less in the lidocaine group than the air and the saline groups.

In the current study, there were significant differences regarding the severity of hoarseness noted by the patient only at 24 hours' post-surgery between the three groups compared to group A. This result is not congruent with the study result of Navarro et al. [31], in which, despite all techniques applied for preventing tracheal morbidity, the incidence of hoarseness was similar in lidocaine and saline groups, suggesting that it is unlikely that this symptom is related to the cuff pressure or to the cuff inflation solution. Our results are consistent with a Kee et al. [24] study which there was found to be a significant difference

between air, dexamethasone and lidocaine groups. Lidocaine and dexamethasone were superior to air at the emergence phase.

Limitation of the current study: The PACU period was short based on the hospital's policies and procedures, which affected the evaluation of cough and prevented an evaluation of sore throat and hoarseness during this time period, as the patient was still unable to speak. Another limitation is that the sample was taken from only one hospital; hence, the results cannot be representative throughout Palestine.

CONCLUSION

The combination of alkalized lidocaine and dexamethasone, or lidocaine alone in the ETT cuff had superior effects in reducing the incidence and the severity of post-extubation morbidities such as cough, sore throat and hoarseness than dexamethasone alone or the control group.

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CONFLICT OF INTERESTS

The authors report no conflicts of interest in this manuscript.

REFERENCES

- 1) Biro P, Seifert B, Pasch T. Complaints of sore throat after tracheal intubation: a prospective evaluation. *Eur J Anaesthesiol* 2005; 22(4): 307-311.
- 2) Fagan C, Frizelle HP, Laffey J, Hannon V and Carey M: The effects of intracuff lidocaine on endotracheal-tube-induced emergence phenomena after general anesthesia. *Anesth Analg* 2000; 91: 201-5.
- 3) Tanaka Y, Nakayama T, Nishimori M, Tsujimura Y, Kawaguchi M, Sato Y. Lidocaine for preventing postoperative sore throat. *Cochrane Database Syst Rev*. 2015; (7): CD004081.
- 4) Soltani HA, Aghadavoudi O. The effect of different lidocaine application methods on postoperative cough and sore throat. *J Clin Anesth*. 2002; 14(1): 15-8.
- 5) Schwilk B, Bothner U, Schraag S, Goergieff M. Perioperative respiratory events in smokers and nonsmokers undergoing general anesthesia. *Acta Anaesthesiol Scand*. 1997; 41: 348-55.
- 6) Jensen PJ, Hommelgaard P, Sondergaard P and Eriksen S: Sore throat after operation: influence of tracheal intubation, intracuff pressure and type of cuff. *Br J Anaesth* 1982; 54: 453-7.
- 7) Stout DM, Bishop MJ, Dwersteg JF and Cullen BF: Correlation of endotracheal tube size with sore throat and hoarseness following general anesthesia. *Anesthesiology* 1987; 67: 419-21.
- 8) El Hakim M: Beclomethasone prevents postoperative sore throat. *Acta Anaesthesiol Scand* 1993; 37: 250-2.
- 9) Shroff P, Patil V. Efficacy of cuff inflation media to prevent postintubation-related emergence phenomena: air, saline and alkalized lignocaine. *Eur J Anaesthesiol* 2009; 26(6): 458-462.
- 10) Steinhaus JE and Gaskin L: A study of intravenous lidocaine as a Suppressant of cough reflex. *Anesthesiology* 1963, 24:285-90.
- 11) Tanaka Y, Nishimori M, Sato Y, Furuya H. Lidocaine for preventing postoperative sore throat. *Cochrane Database Syst Rev*. 2009; 8: CD004081.
- 12) Hirota W, Kobayashi W, Igarashi K, Yagihashi Y, Kimura H, Strupish J, et al. Lidocaine added to a tracheostomy tube cuff reduces tube discomfort. *Can J Anaesth*. 2000; 47: 412-4.
- 13) Estebe JP, Gentili M, Le Corre P, Dollo G, Chevanne F, Ecoffey C. Alkalinization of intracuff lidocaine: efficacy and safety. *Anesth Analg* 2005; 101(5): 1536-1541.
- 14) Rafiei MR, Arianpour N, Rezvani M, Ebrahimi A. Effects of intracuff dexamethasone on post-extubation reactions. *J Res Med Sci*, 2012; 17: 338-43.
- 15) Jarahzadeh MH, Fuladgar B, Mirjalili MR, Rahimi-Bashar F, Dehghani MH, Barzegar K. Effect of local application

- of dexamethasone on reducing of post-surgical sore throat due to application of laryngeal mask airway. *J Biol Today's World*. 2014; 3: 271–274.
- 16) Banihashem N, Alijanpour E, Hassannasab B, Zarei A. Prophylactic effects of lidocaine or beclomethasone spray on post-operative sore throat and cough after orotracheal intubation. *Iran J Otorhinolaryngol*. 2015; 27: 179–184.
- 17) Ayoub MC, Ghobashy A, McGrimely L, et al. Wide spread application of topical steroids to decrease sore throat, hoarseness and cough after tracheal intubation. *Anesth Analg* 1998; 87(3): 714-716.
- 18) Sumathi PA, Shenoy T, Ambareesha M, Krishna HM. Controlled comparison between betamethasone gel and lidocaine jelly applied over tracheal tube to reduce postoperative sore throat, cough, and hoarseness of voice. *Br J Anaesth* 2008; 100(2): 215-218.
- 19) Park SH, Han SH, Do SH, Kim JW, Rhee KY, Kim JH. Prophylactic dexamethasone decreases the incidence of sore throat and hoarseness after tracheal extubation with a double-lumen endobronchial tube. *Anesth Analg* 2008; 107(6): 1814-1818.
- 20) Tazeh-kand NF, Eslami B, Mohamadian K. Inhaled fluticasone propionate reduces postoperative sore throat, cough and hoarseness. *Anesth Analg* 2010; 111(4): 895-889.
- 21) Jiménez-Rodríguez RM, Rubio-Dorado-Manzanares M, Díaz-Pavón J M, Reyes-Díaz M L, Vazquez-Monchul JM, Garcia-Cabrera AM, De la Portilla F. Learning curve in robotic rectal cancer surgery: current state of affairs. *Int J Colorectal Dis* 2016; 31(12): 1807-1815.
- 22) Navarro LHC, Aguiar AS, Braz JRC, Carness JM, Módolo NSP. The effect of intracuff alkalized 2% lidocaine on emergence coughing, sore throat, and hoarseness in smokers. *Rev Assoc Med Bras* 2012 ; 58(2): 248-253.
- 23) Ali NP, Tauhid-ul-Mulck M, Noor M, Mollick MT, Ahmed M, Chowdhury MRA. Lidocaine as endotracheal tube cuff inflating agent. *Journal of Armed Forces Medical College, Bangladesh* 2009 ; 5(1): 25-28.
- 24) Kee K, Nadia M, Melvin K, Muhammad M, Raha, A, Nurlia Y. Post-Intubation Airway Related Adverse Effects: A Comparison between Intra-Cuff Dexamethasone and Intra-Cuff Alkalized Lignocaine. *J Surg Acad* 2013; 3(2): 26-31.
- 25) Choubsaz M, Amirifard N, Sadeghi M, Sadeghi E, Johari Z. The effect of adding dexamethasone to intracuff lidocaine 2% on decreasing the respiratory complications after general anesthesia: a randomized, double blind, clinical trail. *J Appl Pharm Sci* 2016; 6(05): 152-155.
- 26) Ahmady MS, Sadek S, Al-metwalli RR. Does intra-cuff alkalized lidocaine prevent tracheal tube induced emergence phenomena in children. *Anaesth Pain Intens Care* 2013; 17(1): 18-21.
- 27) Cho CK, Kim JE, Yang HJ, Sung TY, Kwon HU, Kang PS. The effect of combining lidocaine with dexamethasone for attenuating postoperative sore throat, cough, and hoarseness. *Anesth Pain Med* 2016; 11(1): 42-48.
- 28) Huang C, Hsu Y, Chen C, Ko Y, Rau R, Wu K, Wei T. Prevention of coughing induced by endotracheal tube during emergence from general anesthesia. a comparison between three different regimens of lidocaine filled in the endotracheal tube cuff. *Acta Anaesthesiol Sin* 1998; 36(2): 81-86.
- 29) Porter N, Sidou V, Husson J. Postoperative sore throat: incidence and severity after the use of lidocaine, saline, or air to inflate the endotracheal tube cuff. *AANA journal* 1999; 67(1): 49-52.

- 30) Ahmady MS, Sadek S, Al-metwalli RR. Does intra-cuff alkalized lidocaine prevent tracheal tube induced emergence phenomena in children. *Anaesth Pain Intens Care* 2013; 17(1): 18-21.
- 31) Navarro LH , Lima, RM, Aguiar AS, Braz JRC, Carness JM, Módolo NSP. The effect of intracuff alkalized 2% lidocaine on emergence coughing, sore throat, and hoarseness in smokers. *Rev Assoc Med Bras* 2012; 58(2): 248-53.
- 32) Zagharnah I, Alkaissi A, Almasri N. The effect of intracuff alkalized lidocaine and dexamethasone on post-extubation morbidities in smoker patients undergoing laparoscopic surgery: A double blind randomized control. 2019. Master thesis, Nursing and Midwifery Department, Faculty of Medicine and Health Sciences. An-Najah National University.