Ekstübasyon Sonrası Görülen Kardiyovasküler ve Solunum Sistemi Yanıtlarına Benzidamin ve Lidokain'in Etkileri

Effects of Benzydamine and Lidocaine on Cardiovascular and Respiratory Responses to Extubation

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ÖZ

GİRİŞ ve AMAÇ: *Endotrakeal tüp kafının (ETT) üzerine benzidamin sprey uygulanması, ameliyat sonrası boğaz ağrısı oranını azaltır. Bu uygulamanın etkinliği, bu amaçla yaygın olarak kullanılan intravenöz lidokain ile karşılaştırılmamıştır. Bu çalışmamızda; entübasyon öncesi endotrakeal tüp kafi çevresine uygulanan benzidaminin ve intravenöz yoldan lidokainin ekstübasyona bağlı kardiyovasküler ve solunum sistemlerinde gelişebilecek olumsuz yanıtlara etkileri araştırıldı.*

YÖNTEM ve GEREÇLER: *İki yüz hasta rastgele 4 gruba ayrıldı (her birinde n = 50). Kontrol grubuna (Grup C) ekstübasyondan 5 dakika önce intravenöz (iv) salin, lidokain grubuna (Grup L) 1,5 mg.kg-1 iv lidokain uygulandı. Benzidamin grubuna (Grup B) ve lidokain-benzidamin grubuna (Grup LB) entübasyondan önce ETT'lerine benzidamin sprey uygulandı, ekstübasyondan 5 dakika önce sırasıyla iv salin ve 1.5 mg.kg-1 iv lidokain uygulandı. Ekstübasyon (1-30 dk) sonrası hemodinamik parametreler ve postoperatif 1-72 saat boğaz ağrısı, öksürük, ses kısıklığı kaydedildi.*

BULGULAR: *Demografik veriler tüm gruplarda benzerdi. Kalp hızındaki artış B ve LB gruplarında C ve L gruplarına göre daha düşüktü (p <0.001). Ortalama arter basıncı değerleri gruplar arasında benzerdi. Postoperatif boğaz ağrısı (1-12 saat), öksürük (1. saat) ve ses kısıklığı (1. saat) görülme sıklığı grup B ve LB'de C ve L gruplarına göre daha düşüktü (p <0.001).*

TARTIŞMA ve SONUÇ: *Hem ekstübasyondan önce iv lidokain uygulanması hem de tek başına veya iv lidokain ile birlikte entübasyondan önce benzidaminin ETT e püskürtülmesi, postoperatif boğaz ağrısı, öksürük ve ses kısıklığını azaltmada etkiliydi. ETT uygulanan topikal benzidamin, postoperatif boğaz ağrısı, öksürük ve ses kısıklığı oranları açısından intravenöz lidokainden üstündü.*

Anahtar Kelimeler: *lidokain, benzidamin, ekstübasyon, hemodinamik yanıt, respiratuvar yanıt*

ABSTRACT

INTRODUCTION: *Benzydamine spray of endotracheal tube cuff (ETTc) supresses postoperative sore throat rate. Efficiency of this practice has not been compared to the common practice of intravenous lidocaine application. Present study aims to compare the efficiency of these practices.*

METHODS: *Two hundred patients were randomized into 4 groups (n=50, in each). Control group (Group C) had iv saline, lidocaine group (Group L) had 1.5 mg.kg-1 iv lidocaine 5 min before extubation. Benzydamine group (Group B) and lidocaine-benzydamine group (Group LB) had their ETTc sprayed with benzydamine before the intubation, iv saline and 1.5 mg.kg-1 iv lidocaine was administered 5 min before the extubation respectively. Hemodynamic parameters after the extubation (1-30 min) and sore throat, coughing, hoarseness at the postoperative 1-72 hrs were recorded.*

RESULTS: *Demographic data were similar. The increase in heart rate was lower in groups B and LB compared to groups C and L (p<0.001). Mean arterial pressure values were similar between the groups. The incidence of postoperative sore throat (1-12hour), coughing (1st hour) and hoarseness (1st hour) were lower in groups B and LB in comparison with groups C and L (p<0.001).*

DISCUSSION AND CONCLUSION: *Both administering iv lidocaine before extubation and administering topical benzydamine on ETTc before entubation either with or without iv lidocaine were effective in decreasing postoperative sore throat, cough and hoarseness rate. Topical benzydamine on ETTc was superior to intravenous lidocaine in terms of postoperative sore throat, cough and hoarseness rates.*

Keywords: *lidocaine, benzydamine, extubation, hemodynamic response, respiratory response.*

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INTRODUCTION

At the end of general anesthesia with endotracheal intubation, reflex cardiovascular responses (tachycardia, arrythmia, increases in arterial blood pressure etc.) and side affects on the respiratory system (coughing, sore throat, hoarseness, laryngo-bronchospasm etc.) are observed following the extubation due to the stimulation of receptors by mechanical and chemical factors found mainly in the trachea and bronchi (1-4).

Keeping the responses of these two systems within physiologic limits helps to avoid or minimize complications. Numerous suggestions have been made concerning the minimalization of these responses (5-7). The most widely used techniques among these suggestions are the application of lidocaine inside or around the cuff or to administer it intravenously (iv) prior to intubation/extubation (7-8-9). Benzydamine, which has antiinflammatory and local anesthetic properties, has been recently demonstrated to decrease the incidence of postoperative sore throat rate (10-12). It had been shown to be effective when applied to laryngeal masks or intraorally or as a spray around the ETT cuff prior to intubation to decrease the incidence of sore throat (13). In a literature review, no study was found comparing the effectiveness of iv. lidocaine before the extubation and topical lidocain on ETTc prior to intubation in order to supress the hemodynamic responses and decrease respiratory side effects.

Thus, this study was designed to evaluate and compare topical benzydamine on the ETTc and iv. lidocaine administration before the extubation for their efficiancy to supress hemodynamic responses and reduce respiratory side effects, either alone or in combination.

METHODS

This study has been carried out in a university hospital Anesthesiology and Reanimation Department, following the approval of Ministry of Health, Clinical Drug Investigations Ethics Committee (Date 23.09.2010, decision number 40). Two hundred patients aged between 18-65 years, belonging to ASA I-II group and scheduled for operations lasting shorter than 2 hour in the supine position were enrolled in this prospective, randomized, placebo controlled study. Exclusion criteria were history of allergies to drugs used in the study, patients with expected difficult intubation, patients who required more than one attempt on intubation, patients with a history of previous neck, trachea and thoracic surgeries, patients with a history of throat or oral pain prior to surgery, patients with hemodynamic instability, increased intracranial pressure, upper respiratory tract or pulmonary infections, pregnant women, morbidly obese and patients who refused to participate in the study. Patients giving written informed consent have been included in the study.

Patients were randomized into four groups (n:50, in each) as follows:

Control Group (Group C) 10 ml iv saline, 5 min. before the extubation,

Lidocaine Group (Group L) 1.5 mg.kg-1 iv lidocaine in 10 ml saline, 5 min. before the extubation,

Benzydamine Group (Group B) 4 puffs of benzydamine spray (1 puff=0.270 mg benzydamine) were applied on the ETTc prior to intubation and 10 ml iv saline 5 min. before the extubation, Lidocaine+Benzydamine Group (Group LB) 4 puffs of benzydamine spray were applied on the ETTc prior to intubation and 1.5 mg.kg-1 lidocaine in 10 ml iv saline 5 min. before the extubation.

Patients did not receive premedication. In the operation room; heart rate (HR), mean arterial pressure (MAP), peripheral oxygen saturation (SpO2) were monitored. Anesthesia was induced with 5-7 mg.kg-1 thiopenthal (Pental 1 g, Ulugay, Istanbul), neuromuscular blockade with iv 0.6 mg.kg-1 rocuronium (Esmeron, Organon, Istanbul) and endotracheal intubation was performed when TOF (TOF-Watch SX, Organon, Ireland) response reached to 0 %. For female and male patients endotracheal tubes with 7.5 mm and 8.5 mm internal diameter were used respectively. Following the intubation, ETTc was inflated using air and endotracheal tube cuff pressure (ETTcp) was set at 20-30 cm H2O with the help of pressure manometer.

Maintenance was carried out using 0.8-1% isoflurane, remifentanil (Ultiva 5mg, GSK) and rocuronium. All patients were ventilated using 40% oxygen in air with 6-8 ml.kg-1 tidal volume as to have an end-tidal carbon dioxide (EtCO2) pressure of 30-35 mmHg. Throughout the surgery HR, MAP, SpO2, EtCO2 and ETTcp were monitorized and recorded. At the end of surgey neuromuscular blockade was antagonized with iv neostigmine 0.05 mg.kg-1 and atropine 0.02 mg.kg-1 when TOF ratio has reached to 70%. HR and MAP values were measured and recorded before iv. administration (bia) and in the 1st and 5th minutes before extubation (be1, be5) in the groups. They were also recorded after the extubation (ae) at the 1st, 5th, 10th, 15th, 20th, 25th and 30th minutes (ae1, ae5, ae10, ae15, ae20, ae25, ae30).

Sore throat (ST) was scored with Postoperative Sore Throat Evaluation Scale , where 0 for no ST, 1 point for ST on questioning only, 2 points if the patient complained of ST, 3 points if there was severe ST or changes in voice. Coughing was scored with Pearson Cough Scale , where 0 counting for no coughing, 1 point for mild coughing, 2 points if there was severe coughing; Hoarseness was scored 0 for no hoarseness, 1 point for hoarseness complaint of patient, 2 points for apparent hoarseness and 3 points for aphonia according to Stout's Hoarseness Scale .

Respiratory complications such as sore throat, coughing, hoarseness, dyspnea, laryngospasm, bronchospasm and stridor, gastrointestinal symptoms such as nausea-vomiting were recorded at postoperative (PO) 1st, 6th, 12th, 24th, 48th and 72th hours.

All of the patients were allowed to receive im. meperidine for the pain in the operation area. All of the patients were followed up for 72 hours both at the ward and home over phone call. Demographic data, ASA classification, duration of anesthesia and surgery were also recorded.

Statistical Analysis

SPSS for Windows v15.0 was used for statistical analysis. Numerical variables were shown as median ± standard deviation (Med±SD), quantitative variables were shown as number (n) and percentage (%). Differences in quantitative variables among groups were evaluated using unidirectional variance analysis (ANOVA) or Kruskal Wallis test depending on the normal distribution of variables while Chi squared test was used to evaluate differences in qualitative variables. Changes in HR, MAP, Aldrete Score, SpO2 values were evaluated using variance analysis in repeated measurements. Differences among groups in sore throat, hoarseness, coughing, dyspnea, laryngospasm and nausea were evaluated using Chi squared test.

RESULTS

There was no statistically significant difference among groups concerning demographic data, ASA status, anesthesia and surgical duration of patients enrolled in the study (Table I). There was no intra or inter-group difference in data of EtCO2, SpO2 or ETTcp values.

Table I. Demographic data, ASA status and anesthesia and surgery durations of cases in groups. [Mean±SD, (Min-Max), (n, %)]

	CG (n=50)	LG (n=50)	BG (n=50)	LBG (n=50)
Age (years)	36.4±12.2 (18-61)	38.4±12.2 (18-62)	37.4±12.8 (19-60)	35.1±13.4 (18-62)
Sex (F/M)	22/28 (%44/%56)	22/28 (%44/%56)	18/32 (%36/%64)	22/28 (%44/%56)
ASA (I/II)	40/10 (%80/%20)	34/16 (%68/%32)	37/13 (%74/%26)	41/9 (%82/%18)
Anesthesia duration (min)	135.4±14.2 (120-190)	132.6±10.8 (120-150)	133.4±10.6 (120-155)	132.1±10.6 (120-150)
Surgery duration (min)	110.2±39.1 (105-180)	119.3±10.3 (110-145)	119.9±10.2 (110-140)	118.9±10.2 (110-140)
***p> 0.05**				

Heart rate values were increased in all of the groups at the measurement time intervals. The increase in the HR values was lower in Group B and LB when compared to the other groups (p<0.001, Figure 1). Group LB had the smallest and Group C had the biggest increase in heart rate. The increase in HR was higher in Group C compared to the HR in Groups L, B and LB (p<0.001, Figure 1.).

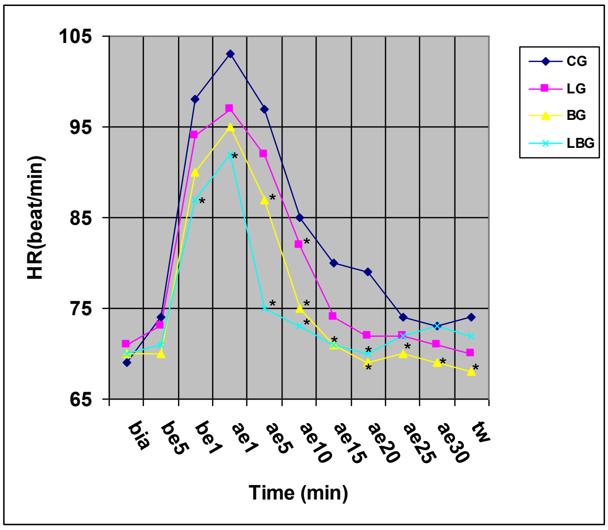

Figure 1: Distribution of the Heart Rate (HR) values in time
***; p<0.001; Compared to Group C**

Table II. Postoperative sore throat incidence according to the groups (n, %)

POST Scale ↓		Group C (n=50)	Group L (n=50)	Group B (n=50)	Group LB (n=50)	P
PO 1hr	0	16 (%32)	42 (%84)*	47 (%94)* #	48 (%96)*ʹ #	<0.001
	1	32 (%64)	7 (%14)	3 (%6)	2 (%4)	
	2	2 (%4)	1 (%2)	0 (%0)	0 (%0)	
	3	0 (%0)	0 (%0)	0 (%0)	0 (%0)	
PO 6 hr	0	23 (%46)	44 (%88)*	50 (%100) *ʹ#	48 (%96)*ʹ #	<0.001
	1	24 (%48)	6 (%12)	0 (%0)	2 (%4)	
	2	3 (%6)	0 (%0)	0 (%0)	0 (%0)	
	3	0 (%0)	0 (%0)	0 (%0)	0 (%0)	
PO 12hr	0	29 (%58)	45 (%90)*	50(%100) *ʹ#	50 (%100) *ʹ #	<0.001
	1	20 (%40)	5 (%10)	0 (%0)	0 (%0)	
	2	1 (%2)	0 (%0)	0 (%0)	0 (%0)	
	3	0 (%0)	0 (%0)	0 (%0)	0 (%0)	
PO 24hr	0	40 (%80)	48 (%96)*	50 (%100)*	50 (%100) *	<0.001
	1	10 (%20)	2 (%4)	0 (%0)	0 (%0)	
	2	0 (%0)	0 (%0)	0 (%0)	0 (%0)	
	3	0 (%0)	0 (%0)	0 (%0)	0 (%0)	
PO 48hr	0	48 (%96)	50 (%100)	50 (%100)	50 (%100)	0.003
	1	2 (%4)	0 (%0)	0 (%0)	0 (%0)	
	2	0 (%0)	0 (%0)	0 (%0)	0 (%0)	
	3	0 (%0)	0 (%0)	0 (%0)	0 (%0)	
PO 72hr	0	50 (%100)	50 (%100)	50 (%100)	50 (%100)	0.425
	1	0 (%0)	0 (%0)	0 (%0)	0 (%0)	
	2	0 (%0)	0 (%0)	0 (%0)	0 (%0)	
	3	0 (%0)	0 (%0)	0 (%0)	0 (%0)	

***; p<0.001; Compared to Group C,**
#; p<0.001; Compared to Groups C and L

In all of the groups MAP values were increased after the extubation in comparison with the values before the extubation in the same group (p<0.001). Inter-group analysis of MAP values did not shown a significant difference (p>0.001), however, Group C had the biggest increase in MAP (Figure 2).

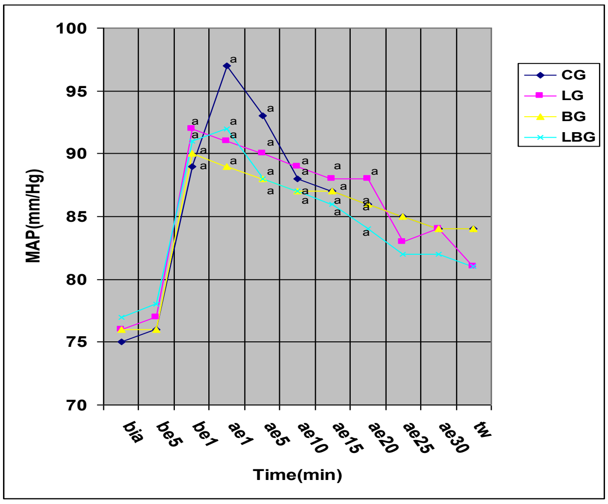

Figure 2: Mean Arterial Pressure (MAP) value distribution in time
a; p<0.001; Intragroup data compared to bia values

Postoperative sore throat incidence data is shown in Table II.

Incidence of postoperative cough at 1st hour were 42%, 48% and 49% in groups C, L, B and LB respectively. The difference in the incidence of postoperative cough at 1st hr was statistically significant between groups C and L, B, LB (p<0.001). Cough incidence in the following 72 hours were similar between the groups. Incidence of hoaserness at postoperative 1st hr was lower in groups B and LB compared to groups C and L (p<0.001) (Table III) .

No dyspnea, laryngospasm, bronchospasm or stridor was observed in any of the patients.

Table III: Incidence of postoperative sore throat (POST), coughing (POC), hoarseness (POH) observed in groups (n,%)

		Ward			Postop. 6.hr.			Postop. 12hr.			Postop. 24.hr.			Postop. 48.hr.		
		POST %	POC %	POH %	POST %	POC %	POH %	POST %	POC %	POH %	POST %	POC %	POH %	POST %	POC %	POH %
CG	0	28[a]	74	88	46[a]	94[a]	96	58[a]	100[a]	98[a]	80[a]	100[a]	100[a]	96[a]	100[a]	100[a]
	1	50	24	8	48	6	4	40	0	2	20	0	0	4	0	0
	2	22	2	4	6	0	0	2	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LG	0	76*	84	94	88[a],*	96[a]	100	90[a],*	100[a]	100	96[a],*	100[a]	100	100[a]	100[a]	100
	1	20	16	6	12	4	0	10	0	0	4	0	0	0	0	0
	2	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BG	0	94*#	96*#	100*	100*#	98	100	100*#	100	100	100[a],*	100	100	100	100	100
	1	6	4	0	0	2	0	0	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LBG	0	96*#	94*#	100*	96*#	98	100	100*#	100	100	100[a],*	100	100	100	100	0
	1	4	6	0	4	2	0	0	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

a; p<0.001; When intragroup data is compared to postoperative ward data *; p<0.001; Compared to group C

#; p<0.001; Group L compared to groups B and LB POST; postoperative sore throat

POC; postoperative coughing POH; postoperative hoarseness

DISCUSSION

Mechanical and chemical factors leads to reflex responses such as a transient increase in the heart rate and blood pressure in the cardiovascular system, sore throat, hoarseness, laryngospasm, bronchospasm and edema in the respiratory system following intubation or extubation (2, 7, 9, 10, 14, 15). The mechanism of these responses is an increase in the plasma concentration of adrenaline, noradrenaline as a result of peripheric sympathoadrenergic stimulation due to the activation of suprasegmental and hypothalamic symphathetical centers in response to impulses generated by sensory nerves found in the oropharynx and nasopharynx, as a reflex-response to the mucosal damage and disruption of mucosal capillary perfusion (3, 8, 11).

Many studies have been carried out to prevent reactions seen in the cardiovascular and respiratory systems after extubation. These can be summarized as systemic administration of NSAIDs, steroids, antihypertensives, antiarrhythmics, opioids and local anesthetics, different anesthetic techniques, extubation under deep anesthesia, usage of special endotracheal tubes in different sizes, application of local anesthetics or lubricant gels around or inside the endotracheal tube cuff or using intraoral lozenges, sprays or mouthwashing (5-8).

Lidocaine is one of the most widely used drugs for preventing cardiovascular or respiratory changes following extubation. The cardiovascular effect of lidocaine is thought to be direct cardiac depression and peripheric vasodilation (14). However, the cardiovascular effects of iv. lidocaine is also related to suppression of coughing (5). Although there are studies reporting that 1-1.5 mg.kg-1 iv. lidocaine before extubation is effective against responses following extubation there are also studies reporting insufficient efficiency and even no efficiency at all (1, 2, 9, 18-21).

The increase in HR and MAP values was observed after the extubation in all of the groups. This increase was significantly less in groups BG and LBG compared to group CG. As a result, this positive effect observed in groups BG and LBG should be caused by benzydamine preventing the tracheal irritation and resultant hemodynamic response. Benzydamine shows antiinflammatory, antiedematous and analgesic effects in inflammations caused by tissue damage by stabilizing the cell membrane, decreasing vascular permeability, without inhibiting prostaglandin synthesis (19-20).

Benzydamine has a more pronounced effect on respiratory responses observed after extubation because there are studies which report that benzydamine decreases postoperative sore throat, postoperative coughing and respiratory complications, similar to our study (11-15). Although there are studies reporting that lidocaine 1.5 mg.kg-1 iv is effective, there are also studies which conclude that it lacks efficiency, similar to our study (8, 24, 25).

In conclusion, benzydamine puff to the ETT cuff with before entubation and administering iv. 1.5 mg.kg-1 lidocaine 5 minute before extubation alone or together were found effective in reducing but not preventing cardiovascular responses; however both technique effectively reduced respiratory side effects.

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