

Inhaled Albuterol, but Not Intravenous Lidocaine, Protects Against Intubation-induced Bronchoconstriction in Asthma

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Background: **The ability of intravenous lidocaine to prevent intubation-induced bronchospasm is unclear. The authors performed a prospective, randomized, double-blind, placebo-controlled trial to test the ability of intravenous lidocaine and inhaled albuterol to attenuate airway reactivity after tracheal intubation in asthmatic patients undergoing general anesthesia.**

Methods: **Sixty patients were randomized to receive either 1.5 mg/kg intravenous lidocaine or saline, 3 min before tracheal intubation. An additional 50 patients were randomized to receive 4 puffs of inhaled albuterol or placebo 15–20 min before tracheal intubation. Anesthesia was induced with propofol. Immediately after intubation and at 5-min intervals, transpulmonary pressure and airflow were recorded, and lower pulmonary resistance (R_L) was calculated. Isoflurane was administered after the initial two measurements to assess reversibility of bronchoconstriction. A bronchoconstrictor response to intubation was defined as R_L greater than or equal to 5 cm $H_2O \cdot l^{-1} \cdot s^{-1}$ in the first two measurements after intubation and R_L subsequently decreasing by 50% or more after isoflurane.**

Results: **The lidocaine and placebo groups were not different in the peak R_L before administration of isoflurane (8.2 cm $H_2O \cdot l^{-1} \cdot s^{-1}$ *vs.* 7.6 cm $H_2O \cdot l^{-1} \cdot s^{-1}$) or frequency of airway response to intubation (lidocaine 6 of 30 *vs.* placebo 5 of 27). In contrast, the albuterol group had lower peak R_L (5.3 cm $H_2O \cdot l^{-1} \cdot s^{-1}$ *vs.* 8.9 cm $H_2O \cdot l^{-1} \cdot s^{-1}$; $P < 0.05$) and a lower frequency of airway response (1 of 25 *vs.* 8 of 23; $P < 0.05$) than the placebo group.**

Conclusions: **Inhaled albuterol blunted airway response to tracheal intubation in asthmatic patients, whereas intravenous lidocaine did not. (Key words: Bronchial; pulmonary; resistance.)**

ASTHMATIC patients undergoing general anesthesia with tracheal intubation are at increased risk for intubation-induced bronchospasm.[1–6] A variety of drugs given perioperatively have been shown to affect the airway response to intubation.[2–4,6–15] Although case reports and randomized studies suggest that intravenous lidocaine causes bronchodilation, the clinical significance of these observations is unclear.[7,9,12,16–25] Furthermore, most studies of the efficacy of intravenous lidocaine in preventing bronchoconstriction have been conducted in animals or in human subjects during controlled laboratory conditions, not during general anesthesia with tracheal intubation.[26] We therefore prospectively studied the effects of intravenous lidocaine in asthmatic patients undergoing general anesthesia with tracheal intubation. When preliminary results failed to show a protective effect, we extended the study to include a test of inhaled albuterol, a drug known to be an effective bronchodilator in asthmatic patients, using the same patient population and study protocol.[2,3,12,14]

Methods

The study was approved by the hospital's ethics and research committee. One hundred ten patients scheduled for elective surgery requiring general anesthesia and tracheal intubation were recruited over an 8-yr period. Informed consent was obtained. All patients had a diagnosis of asthma by their primary care physician for at least 1 yr, and all had been treated for reactive airways disease with inhaler therapy in the month before surgery. Patients with significant cardiac disease or those requiring awake or fiberoptic intubation were excluded. Patients were instructed not to take any of their regular asthma medicines on the day of surgery. Patients were without asthma medicine for at least 10 h. Patients were given routine spirometry (unless they had had spirometry within 3 months of surgery).

Our study tested the ability of two drugs to protect against intubation-induced bronchoconstriction: part 1 tested the efficacy of intravenous lidocaine, and part 2 tested the efficacy of inhaled albuterol. Part 2 was performed after the completion of part 1. Each part was a randomized, double-blind, placebo-controlled trial. Study drug or placebo was dispensed by the pharmacy and administered to the patient at the predetermined time.

To assess the protective effect of drugs and placebos, we measured lower pulmonary resistance (R_L). Because of the relatively high and variable resistance of the upper airway, we could not make meaningful comparisons of resistance measured before and after intubation. We therefore had to infer the occurrence of intubation-induced bronchoconstriction from measurements made entirely after intubation, *i.e.*, after the event we were detecting. We reasoned that significant bronchoconstriction caused by intubation would result in a relatively high resistance immediately after intubation, and that

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such acutely increased resistance might diminish with time and with the inhalation of isoflurane, an anesthetic agent known to be a brochodilator.[10,14,15] Therefore, patients with high pulmonary resistance ($R_L \geq 5$ cm $H_2O \cdot l^{-1} \cdot s^{-1}$) before administration of isoflurane, whose resistance subsequently decreased by 50% or more while breathing isoflurane, were deemed to have "responded" to intubation with bronchoconstriction. Patients treated with a protective drug would be less likely than those treated with placebo to show a response.

Transpulmonary pressure was measured with a differential transducer (model LCVR; Celesco, Canoga Park, CA) connected between an esophageal balloon catheter and a tracheal catheter positioned at the tip of the endotracheal tube (Portex Jet Ventilator Adaptor; SIMS Portex Ltd., Hythe, UK). The esophageal balloon was 12 cm long, 3 cm in perimeter, and mounted on a polyethylene catheter (2.80-mm OD, 1.77-mm ID). Airflow was measured with a pneumotachometer (Fleisch No. 1; Rusch, Inc., Duluth, GA) and pressure transducer. The flow signal was integrated electrically to indicate volume and calibrated with a 3-l syringe. At prescribed times after intubation, pressure, flow, and volume signals were displayed as pressure–volume and flow–volume traces on a storage oscilloscope, photographed, and later analyzed by the method of Neergard and Wirtz.[3,10,20] We calculated R_L (excluding the upper airway) as the pressure difference between inspiration and expiration at midtidal volume divided by the corresponding flow difference, as previously described.[3,10,20] Traces were very consistent from breath to breath, and we analyzed one representative breath at each time point.

In part 1, intravenous lidocaine (1.5 mg/kg) or saline was given as a bolus dose 2.5–3 min before planned intubation. In part 2, albuterol or albuterol–placebo was administered in four puffs from a metered dose inhaler, 15–20 min before planned intubation. All patients were premedicated with midazolam (1–2 mg administered intravenously), and after standard noninvasive monitoring was applied, they were given 100% oxygen to breathe. Anesthesia was induced with propofol (2 mg/kg), fentanyl (3 μg/kg), and vecuronium (0.1 mg/kg) and was maintained with a propofol infusion (100–200 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and 50% nitrous oxide in oxygen by mask. In part 1, intravenous drugs were administered in the following order: fentanyl, propofol, vecuronium, study drug. All patients underwent laryngoscopy and tracheal intubation within 3 min of the start of induction. After laryngoscopy and tracheal intubation (7.5-mm endotracheal tube for men and 7.0 mm for women), an esophageal balloon catheter was positioned with its tip 40 cm from the incisors, and the tracheal catheter was advanced to the distal endotracheal tube.

Patients underwent ventilation with equal parts oxygen and nitrous oxide (50/50), using tidal volumes of 10 ml/kg at 8 breaths/min using a square waveform inspiratory flow (Ohmeda Anesthesia Ventilator 7800 series; Datex-Ohmeda, Madison, WI). Respiratory measurements were made as soon as possible after intubation, within 1 min, and at approximately 5-min intervals thereafter for a total of five measurements. Surgical preparation and draping were allowed to begin after obtaining the first two measurements and the start of isoflurane. Heart rate and mean systemic blood pressure were also recorded. After the initial two measurements, isoflurane inhalation (2% inspired concentration) was begun, and the propofol infusion was discontinued. After three more measurements, the study protocol was finished, and respiratory measuring equipment was removed.

Statistical Analysis

Data are presented as mean, SD, median, and range, or as number and percent of patients. For each phase of the study, treated and placebo groups were compared with respect to preoperative respiratory variables, intraoperative hemodynamic and pulmonary measurements, and R_L using a two-sample *t* test (age, weight, mean blood pressure), Wilcoxon rank sum test (forced expiratory volume in 1 s [FEV_1], heart rate, R_L), or the Fisher exact test (sex, asthma medications). To compare changes in hemodynamic parameters, the number of patients whose postintubation heart rate and mean blood pressure measurements changed by more than 20% from preintubation were compared between groups using the Fisher exact test. The effects of isoflurane were assessed within each group by comparing the difference between maximum preisoflurane and minimum postisoflurane R_L using the Wilcoxon signed rank test.

Subjects were originally categorized as responders if the maximum R_L in the first two measurements after intubation, and before administration of isoflurane, was greater than or equal to 5 cm $H_2O \cdot l^{-1} \cdot s^{-1}$ and subsequently decreased by 50% or more while breathing isoflurane. In a *post hoc* analysis, we explored secondary definitions of response, as described in Results. Response rates of treated and placebo patients were compared using the Fisher exact test.

Results

Figure 1 shows R_L changes after intubation in a representative patient who met the original definition of response to intubation and in a patient who did not. The initially high pulmonary resistance progressively diminished with time or the start of isoflurane administration.

Although several patients recorded high pulmonary resistances and evidence of expiratory obstruction, only one patient (intravenous lidocaine study group) demonstrated severe bronchoconstriction requiring albuterol treatment and early administration of isoflurane. In this patient we were able to obtain one measurement before

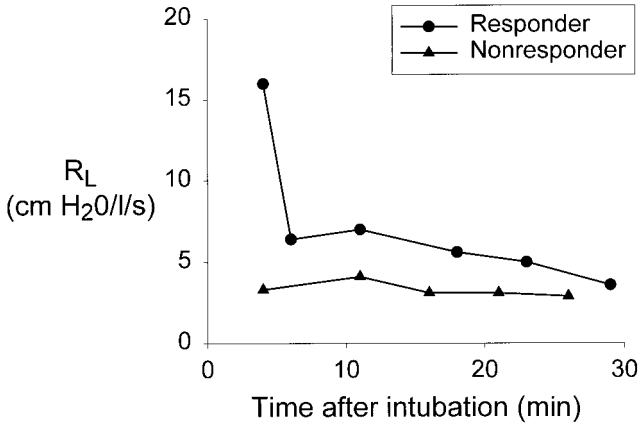

Fig. 1. Lower pulmonary resistance (R_L) after intubation in two patients, one who responded to intubation with bronchospasm and another who did not. Isoflurane inhalation begins after the second measurement in each patient.

rescue therapy. This patient had received intravenous lidocaine and was listed as a responder.

Part 1: Lidocaine–Placebo

Sixty patients were randomized, 30 in each group. Three patients receiving placebo were excluded from analysis, two because of change in the anesthetic plan (no tracheal intubation necessary) and one because of inadequate oscilloscope records. There were no significant differences between lidocaine and placebo groups in preoperative patient characteristics, preoperative FEV_1, or percent change in FEV_1 after bronchodilation. There were no differences in preintubation hemodynamic values or in the proportion of patients whose heart rate or mean blood pressure changed by more than 20% with intubation, suggesting that the groups were anesthetized to similar depth (table 1).

There was no significant difference in R_L measurements after intubation and before isoflurane (mean R_L, 8.2 [SD 9.1] cm $H_2O \cdot l^{-1} \cdot s^{-1}$ for lidocaine, 7.6 [SD 6.7] cm $H_2O \cdot l^{-1} \cdot s^{-1}$ for placebo; table 1 and fig. 2). There was also no significant difference in R_L measurements after the administration of isoflurane (4.3 [SD 3.6] cm $H_2O \cdot l^{-1} \cdot s^{-1}$ for lidocaine *vs.* 4.3 [SD 4.5] cm $H_2O \cdot l^{-1} \cdot s^{-1}$ for placebo). In addition, there was no significant difference in the rate of response to tracheal intubation (table 2 and fig. 3).

Part 2: Albuterol–Placebo

Fifty patients were randomized, 25 in each group. Two patients receiving placebo were excluded from analysis, one because of change in the anesthetic plan (no tracheal intubation necessary) and one because of inadequate measurements. The median FEV_1 during preoperative evaluation was significantly greater in the albuterol group (102% *vs.* 90% of predicted; $P = 0.04$). However, the change in FEV1 (%) after bronchodilation was not different between the two groups. There were no differences in preintubation hemodynamic values or in the number of patients whose heart rate or mean blood pressure changed by more than 20% with intubation (table 1).

The R_L after intubation and before isoflurane was lower in the treated group (mean R_L, 5.3 [SD 3.0] cm $H_2O \cdot l^{-1} \cdot s^{-1}$ for albuterol, 8.9 [SD 7.4] cm $H_2O \cdot l^{-1} \cdot s^{-1}$ for placebo; $P = 0.04$; table 1 and fig. 2). Although the R_L after intubation was also lower for the albuterol group, it was not statistically significant (3.8 [SD 1.8] cm $H_2O \cdot l^{-1} \cdot s^{-1}$ for albuterol *vs.* 4.9 [SD 2.7] cm $H_2O \cdot l^{-1} \cdot s^{-1}$ for placebo). There were significantly fewer responders (original definition) in the albuterol group: 1 *versus* 8 ($P < 0.01$; table 2 and fig. 3).

Effects of Isoflurane

There were statistically significant reductions in R_L after the administration of isoflurane in all study groups (table 1 and fig. 2). The reduction in R_L was not significantly greater in the intravenous lidocaine group and both placebo groups compared with the albuterol group (albuterol *vs.* inhaled placebo, $P = 0.05$; albuterol *vs.* lidocaine or intravenous placebo, $P > 0.05$).

Secondary Definitions of Response

In determining the protective effect of a drug, our choice of definition of response to intubation was critical because inappropriate criteria for response could obscure differences between groups. Therefore, we performed *post hoc* examination of the ability of other definitions of response to reveal hidden effects. We varied the definition of "high" resistance in the initial measurements from 5 to 3 cm $H_2O \cdot l^{-1} \cdot s^{-1}$ and analyzed the data using 3 cm $H_2O \cdot l^{-1} \cdot s^{-1}$. It also seemed possible that intubation-induced bronchoconstriction might not resolve with time and isoflurane inhalation; therefore, we combined criteria for response to include patients whose initial R_L and minimal R_L after isoflurane were both greater than 5 or 7 cm $H_2O \cdot l^{-1} \cdot s^{-1}$. The results were not different with any of the secondary definitions of response (table 2 and fig. 3).

In our study, 19 of 105 patients (18%) smoked tobacco. Smokers were not significantly different from nonsmokers in R_L before isoflurane (mean R_L of nonsmokers, 7.3 [SD 7.3] cm $H_2O \cdot l^{-1} \cdot s^{-1}$ *vs.* 8.2 [SD 5.8] cm $H_2O \cdot l^{-1} \cdot s^{-1}$ for smokers), R_L after isoflurane (mean R_L of nonsmokers, 4.2 [SD 3.4] cm $H_2O \cdot l^{-1} \cdot s^{-1}$ *vs.* 4.8 [SD 2.8] cm $H_2O \cdot l^{-1} \cdot s^{-1}$ for smokers), or rate of response to intubation. The study groups were not different regarding tobacco use or R_L measured in smokers and nonsmokers before or after administration of isoflurane.

Depth of anesthesia, as inferred from the stability of heart rate and mean blood pressure, was similar in drug and placebo groups in which similar numbers of patients demonstrated 20% change in heart rate or mean blood pressure. For each part of the study, no association was

Table 1. Preoperative Respiratory Evaluation and Intraoperative Hemodynamic and Pulmonary Data for the Lidocaine and Albuterol Study Phases

Patient Demographics, Hemodynamics, and Pulmonary Resistances	Lidocaine (n = 30)	*P*	Placebo (n = 27)	Albuterol (n = 25)	*P*	Placebo (n = 23)
Preoperative FEV_1 (% predicted (SD))	0.85 (0.26)	NS	0.92 (0.21)	0.98 (0.20)	0.04	0.90 (0.14)
Change after bronchodilator (% (SD))	9 (12)	NS	10 (21)	6 (9)	NS	7 (11)
Age (yr (SD))	41.5 (8.3)	NS	44.9 (8.2)	42.8 (9.2)	NS	42.5 (8.0)
Sex (n male (%))	7 (23%)	NS	6 (22%)	6 (24%)	NS	6 (26%)
Weight (kg (SD))	69.2 (9.4)	NS	69.6 (7.4)	71.7 (10.6)	NS	74.7 (6.9)
Tobacco (n (%))	5 (17%)	NS	5 (19%)	5 (20%)	NS	4 (17%)
Asthma medications (n (%))						
β Agonists	30 (100%)	—	27 (100%)	25 (100%)	—	23 (100%)
Ipratropium	5 (17%)	NS	4 (15%)	3 (12%)	NS	4 (17%)
Steroids	4 (13%)	NS	4 (15%)	4 (16%)	NS	4 (17%)
Asmacort	3		4	3		3
Prednisone	1		0	1		1
Preintubation hemodynamics (mean (SD))						
HR (beats/min)	78.1 (13.2)	NS	75.9 (13.2)	77.9 (14.3)	NS	80.5 (13.9)
MBP (mmHg)	82.6 (13.8)	NS	83.0 (14.0)	80.4 (12.3)	NS	81.9 (11.8)
Postintubation hemodynamics (mean (SD))						
HR (beats/min)	85.1 (15.5)	NS	77.6 (15.7)	78.1 (11.1)	NS	80.2 (12.7)
MBP (mmHg)	90.6 (18.1)	NS	87.1 (15.0)	80.4 (11.3)	NS	77.7 (12.6)
% Change hemodynamics (mean (SD))						
HR	10.8 (22.7)		2.7 (15.6)	1.7 (12.2)		0.5 (11.0)
MBP	11.5 (24.7)		7.7 (24.1)	1.5 (12.6)		−4.5 (12.3)
Change HR ≥20% (n (%))	11 (37%)	NS	7 (26%)	2 (8%)	NS	2 (9%)
Change MBP ≥20% (n (%))	11 (37%)	NS	11 (41%)	4 (16%)	NS	2 (9%)
Pulmonary resistance ($l \cdot cm\ H_2O^{-1} \cdot s^{-1}$)						
Postintubation/preisoflurane						
Initial R_L						
(Mean (SD))	7.8 (9.2)	NS	7.2 (6.7)	4.8 (3.0)	0.04	7.3 (5.5)
(Median (range))	4.9 (1.0–44.9)		4.3 (0.8–23.6)	3.8 (1.5–16.0)		6.1 (1.8–28.8)
Max R_L						
(Mean (SD))	8.2 (9.1)	NS	7.6 (6.7)	5.3 (3.0)	0.04	8.9 (7.4)
(Median (range))	6.6 (1.0–44.9)		4.3 (0.8–23.6)	4.0 (2.2–16.0)		6.1 (1.8–34.3)
Postisoflurane R_L						
(Mean (SD))	4.3 (3.6)	NS	4.3 (4.5)	3.8 (1.8)	NS	4.9 (2.7)
(Median (range))	3.5 (0.8–19.5)		2.9 (0.6–21.5)	3.6 (1.5–9.3)		4.1 (1.0–11.5)

Pulmonary resistances (R_L), performed after intubation, are presented for pre- and postisoflurane measurements. For preisoflurane measurements, data include the initial R_L and the greater of the two measurements obtained before isoflurane (max R_L). Values are presented as mean (SD) or number (% of total). For lower pulmonary resistance, the median range are presented below.

* $P < 0.01$ compared with preisoflurane data.

FEV_1 = fractional expiratory volume in 1s; HR = heart rate; MBP = mean blood pressure; postintubation R_L = measured airway resistance (R_L) immediately after intubation and before administration of isoflurane (Forane); Postisoflurane R_L = measured airway resistance after administration of isoflurane.

found between changes in heart rate or mean blood pressure and response to intubation. Similarly, there was no association between preoperative FEV_1 or change in FEV_1 after bronchodilator and airway response to intubation.

Discussion

Our results show that intravenous lidocaine, 1.5 mg/kg, given within 3 min before intubation, was not effective in preventing postintubation bronchospasm in asthmatic patients undergoing general anesthesia with tracheal intubation after a propofol induction. However, inhaled albuterol was effective. The efficacy of albuterol was expected, as it is an effective bronchodilator in patients with asthma and in the setting of general anesthesia with tracheal intubation.[2,3,13,14,24] By contrast, although intravenous lidocaine has been described as useful in preventing intubation-induced bronchospasm,[2,20,24] its efficacy is less well established.[26] Previous studies demonstrating bronchodilation after intravenous lidocaine did so either in nonintubated patients or during provocative tests after intubation and stabilization.[15,20,23–25,27,28] Other studies demonstrating beneficial effects of lidocaine on tracheal muscle tone were performed *in vitro*.[17,19,21] Intravenous lidocaine alone has been shown to have minimal effects on bronchial tone.[23,24,29,30] In the setting of a histamine challenge, doses up to 10 mg/kg may even result in airway narrowing consistent with bronchoconstriction,[25] although bronchodilation may result with similar doses after methacholine challenge.[31]

Recommendations for the use of intravenous lidocaine have been based principally on laboratory investigations in humans or animals or *in vitro* experiments.[17–24,27,31]

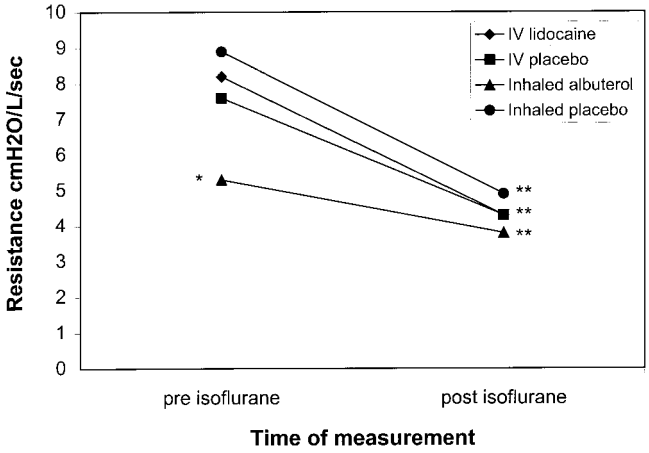

Fig. 2. Mean lower pulmonary resistance (R_L) before and after the administration of isoflurane from each of the four study groups. Patients receiving albuterol had a significantly lower preisoflurane R_L compared with inhaled placebo (*$P < 0.05$). R_L was significantly lower after isoflurane in all study groups ($P < 0.05$). IV = intravenous.**

Several of these studies have tested the efficacy of intravenous lidocaine in the setting of direct or indirect airway irritants such as histamine,[7,24,25,27,28] acetylcholine or methylcholine,[29,31] or mechanical irritants such as distilled water or inhaled lidocaine.[12,22] Few, if any, studies have tested the benefits of prophylactic lidocaine in the setting of intubation-induced bronchoconstriction. Of the studies assessing the affects of lidocaine on airway tone in asthmatic patients, none involved general anesthesia with intubation, and only three examined intravenous lidocaine.[9,11,23,24,28] Inhaled lidocaine administered to asthmatic patients is reported to cause increased bronchomotor tone or constriction, whereas intravenous lidocaine was reported to cause bronchodilation.[9,11,23,24,28]

Although our results show no benefit of lidocaine in these conditions, it must be recognized that our data may have been affected by the anesthetic regimen used. Opioids have been shown to inhibit airway responses to a variety of stimuli.[32–34] Likewise, propofol has been shown to attenuate airway response to a variety of stimuli compared with thiobarbiturates, the latter of which is commonly used in both clinical practice and studies of bronchial response.[4,6,12,15,22,35] Eames *et al.*[6] reported a postintubation R_L of 8.1 cm $H_2O \cdot l^{-1} \cdot s^{-1}$ after propofol compared with 11.3 cm $H_2O \cdot l^{-1} \cdot s^{-1}$ for thiopental. In the present study, in which propofol was used in all patients, immediate postintubation R_Ls were similar to that reported by Eames *et al.* for all groups except the albuterol group, in which it was lower, suggesting that albuterol adds significantly to the previously demonstrated protective effect of propofol.[6] This was also demonstrated in a recent investigation by Wu *et al.*[36] In this study, fenoterol, and not ipratropium, was effective in decreasing respiratory resistance after intubation in patients anesthetized with propofol. The investigators noted that use of propofol did not prevent increased resistance immediately after intubation, and that the "protection was not absolute in asthmatic patients."[36] Finally, the addition of isoflurane resulted in a small but significant reduction of R_L in the albuterol group, a result that has been demonstrated elsewhere.[13,14]

Another variable among investigations is the dose and timing of intravenous lidocaine. Doses ranging from 1 to 10 mg/kg, with and without infusions, have been administered from 1 to 10 min before laryngoscopy and intubation with a wide range of effects on hemodynamic changes, the cough reflex, and pulmonary resistance. In the current study, a dose of 1.5 mg/kg intravenous lidocaine was administered within 3 min of intubation. Other studies have shown similar dosing to be effective in reducing the minimal alveolar–anesthetic concentration of inhalation agents,[37] blunting hemodynamic changes with laryngoscopy and intubation,[8,38,39] attenuating the cough reflex,[12,40,41] and decreasing bronchomotor tone, *i.e.*, bronchodilation.[24] On the other hand, two studies have not demonstrated a significant

Table 2. Incidence of Responses to Tracheal Intubation According to Primary and Secondary Definitions of a Response

Criteria	Lidocaine (n = 30)	*P*	Placebo (n = 27)	Albuterol (n = 25)	*P*	Placebo (n = 23)
Original criteria for response						
Preisoflurane R_L ≥5 and 50% decrease	6 (20)	1.0	5 (19)	1 (4)	0.009	8 (35)
Secondary criteria						
Preisoflurane R_L ≥3 and 50% decrease	8 (27)	1.0	7 (26)	1 (4)	0.009	8 (35)
Preisoflurane R_L ≥3 and 50% decrease *and*						
Preisoflurane R_L and postisoflurane R_L ≥5	16 (53)	0.6	12 (44)	5 (20)	0.034	12 (52)
Preisoflurane R_L and postisoflurane R_L ≥7	11 (37)	0.8	11 (41)	2 (8)	0.003	11 (48)
Preisoflurane R_L ≥5 and 50% decrease *and*						
Preisoflurane R_L and postisoflurane R_L ≥5	14 (47)	0.6	10 (37)	5 (20)	0.034	12 (52)
Preisoflurane R_L and postisoflurane R_L ≥7	9 (30)	1.0	9 (33)	2 (8)	0.003	11 (48)

Data are presented as number of responders in each subgroup (percentage of group) for each definition of a responder. Airway resistance (R_L) is recorded in $l \cdot cm\ H_2O^{-1} \cdot s^{-1}$. Preisoflurane resistance (R_L) refers to the greater of two measurements performed after intubation and before administration of isoflurane. A decrease in R_L refers to a ≥ 50% decrease in R_L measurements obtained after administration of isoflurane. The secondary definitions were created to account for those patients who may have had increased R_L before *and* after isoflurane because it was possible for a patient to have bronchoconstriction that did not resolve during the study period. The data were also evaluated with an R_L of 3 $l \cdot cm\ H_2O^{-1} \cdot s^{-1}$ considered as increased.

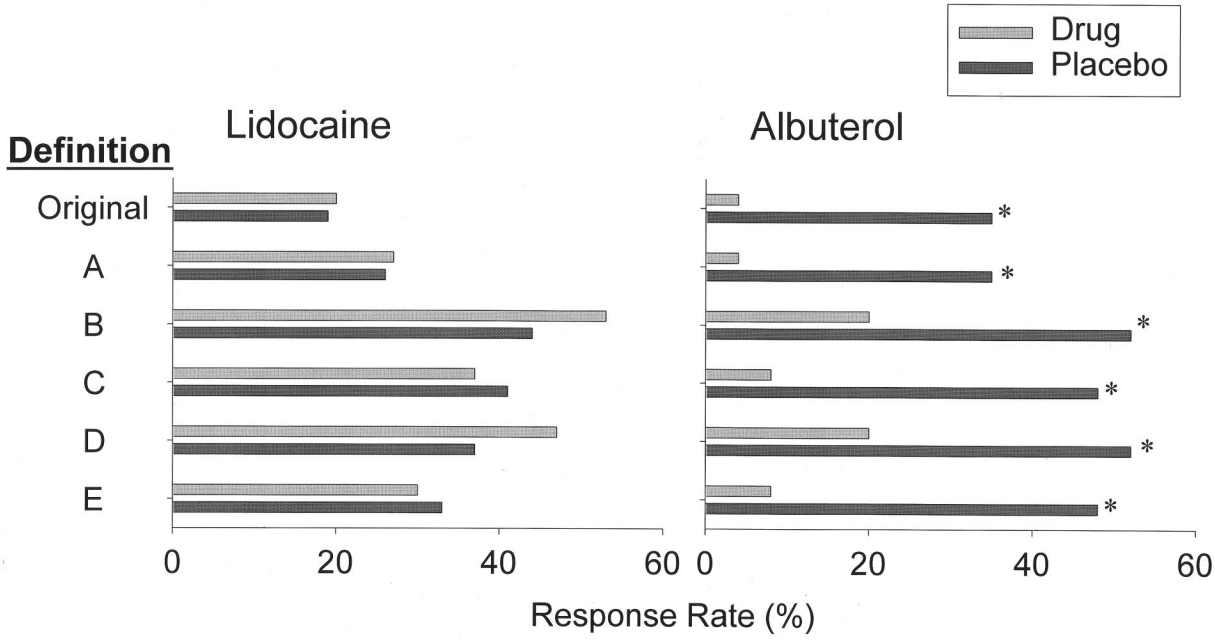

Fig. 3. Response frequency among drug and placebo groups using the original definition of response and secondary definitions (*A–E*) described in table 2. Intravenous lidocaine was not different from placebo in preventing intubation-induced bronchospasm by any definition. Albuterol was significantly (P* < 0.05) better than placebo using the original definition or secondary definitions of response.**

benefit from this dose of intravenous lidocaine.[29,42] Furthermore, Hirota *et al.*[25] demonstrated a reduction in bronchial area, *i.e.*, bronchoconstriction, with doses of 1 or 10 mg/kg intravenous lidocaine. Yokioka *et al.*[40] studied doses ranging from 0.5 to 2.0 mg/kg given 1–15 min before intubation and concluded that 1.5 mg/kg or greater given 1–3 min before airway stimulation suppressed the cough reflex.

We did not demonstrate any significant effect of tobacco use on the airway response to tracheal intubation. Although other studies have shown that tobacco use may increase airway response to intubation, the relative airway effects between tobacco and preexisting asthma are unknown.[3,6] We also did not demonstrate any association between preoperative FEV_1, or change in FEV_1 after bronchodilation, and bronchial response to intubation. Our data suggest that preoperative FEV_1 may not be useful in predicting which patients may exhibit bronchoconstriction with intubation. This is not surprising because asthma is an episodic disease. During preoperative testing, patients are in a stable condition. At this point a known bronchodilator may not have any significant change on airflow and may therefore not be predictive of response to a noxious stimuli such as an endotracheal tube. Provocative testing before intubation may have been a better indicator of airway response to a noxious stimuli.

Sample size may be a limitation for the first part of the study. It is not known what fraction of asthmatic patients show clinically significant bronchoconstriction in response to tracheal intubation. In part 1, the response rate (original definition) was approximately 20% in both groups, whereas the response rate in the placebo group in part 2 was 35%. From our data, we cannot exclude the possibility that lidocaine had a small but clinically significant effect. For example, if lidocaine reduced the incidence of response from 35% to 20%, we would have needed approximately 140 patients per group to have an 80% chance of demonstrating an effect. With 30 patients in each group, a study has an 80% chance of detecting a reduction in response from, for example, 35% to 6.5% or from 30% to 3.5%, which is similar to the response rates in the second phase of our study.

In conclusion, our study demonstrates that intravenous lidocaine was not effective in reducing the airway responsiveness to tracheal intubation. Despite a number of studies showing bronchodilation after administration of both intravenous and topical local anesthetic agents, no study has demonstrated a protective effect of these agents in preventing bronchospasm after intubation in patients undergoing general anesthesia. Our study also showed that inhaled albuterol is effective in reducing airway responsiveness to intubation, in agreement with previous studies. Given the lack of effect of intravenous lidocaine (1.5 mg/kg) as well as an absence of convincing data in the literature, we do not recommend the routine use of intravenous lidocaine to reduce bronchospasm after tracheal intubation, at least in patients given propofol. However, inhaled albuterol is effective for this purpose.

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