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Nicardipine versus lidocaine for attenuating the cardiovascular response to endotracheal intubation

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Abstract

Purpose. The aim of this study was to compare the efficacy of nicardipine and lidocaine in attenuation of cardiovascular responses to endotracheal intubation.

Methods. In a randomized, double-blind, controlled trial, 60 unpremedicated (ASA I) patients undergoing elective surgery were given either 30 μg·kg^{-1} nicardipine or 1.5 mg·kg^{-1} lidocaine intravenously 2 min before intubation. Laryngoscopy and tracheal intubation were performed 1 min after induction of anesthesia with 5 mg·kg^{-1} thiopentone, followed by administration of 1.5 mg·kg^{-1} succinylcholine intravenously. Blood pressure and heart rate were monitored at baseline and every minute until 4 min after intubation. Repeated-measures ANOVA, Student's *t* test, the chi-square test, and 95% confidence intervals were used as appropriate. $P < 0.05$ was considered statistically significant.

Results. Baseline hemodynamic variables were not different between the groups. After administration of either agents, diastolic blood pressure and mean blood pressure were significantly lower in the nicardipine group. The heart rate in the nicardipine group was significantly higher. The mean between-group differences in diastolic blood pressure, mean blood pressure, heart rate, and rate-pressure product at baseline and 1 min after starting laryngoscopy were statistically significant.

Conclusion. Nicardipine can be used as an alternative to lidocaine in attenuation of cardiovasculars response to tracheal intubation in patients without ischemic heart disease.

Key words: Nicardipine, Lidocaine, Cardiovascular response, Intubation

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Introduction

Laryngoscopy and tracheal intubation after a standardized induction dose of thiopentone often provokes a reflex increase in both sympathetic and sympathoadrenal activity, which may result in hypertension, tachycardia, and arrhythmias [1–6]. These responses, although transient, may be harmful in some patients, particularly those suffering from myocardial or cerebrovascular disease. Many pharmacological techniques, including the use of opioids, local anesthetics, adrenergic blocking agents, and vasodilating agents such as nitroglycerine and sodium nitroprusside, have been devised to reduce the extent of the hemodynamic events [1–3,7–10]. Lidocaine hydrochloride, an aminoethylamide local anesthetic and class IB antidysrhythmic agent, is an acceptable agent for attenuation of the cardiovascular response to intubation and will also diminish cough reflexes, dysrhythmias, and rises in intracranial and intraocular pressure [10]. Kyokong et al. showed that 1.5 mg·kg^{-1} lidocaine administered intravenously 2 min before intubation could attenuate the cardiovascular response to laryngoscopy and intubation [11]. Nicardipine is a new dihydropyridine derivative that acts as a calcium channel blocker. Nicardipine produces an immediate, short-acting, reliable reduction in blood pressure without adverse effects such as hypotension, disturbances of atrioventricular conduction, and myocardial depression [12,13]. Moreover, it produced consistent augmentation of coronary blood flow, oxygen delivery, and aerobic metabolism in ischemic myocardium [14]. Omote showed that 20 or 30 μg·kg^{-1} nicardipine was effective in preventing the circulatory responses to laryngoscopy and tracheal intubation in normotensive and hypertensive patients [15]. However there was no separate study comparing the effects of intravenous lidocaine and nicardipine. This study aimed to compare the efficacy of single rapid administration of lidocaine and nicardipine for controlling these hemody-

namic responses to tracheal intubation under the same anesthetic technique.

Methods

The study was approved by the Ethical Committee of the Faculty of Medicine, Chulalongkorn University. We studied 60 normotensive patients (ASA I) undergoing elective surgery, all of whom had given informed consent. The patients were randomly allocated into two groups (n = 30 for each group) to receive nicardipine 30 μg·kg^{-1} or lidocaine 1.5 mg·kg^{-1} intravenously. Patients who were suspected to have difficult tracheal intubation or who had hypertension (systolic blood pressure >160 mmHg and/or diastolic blood pressure >95 mmHg as defined by the World Health Organization), renal, hepatic, or gastrointestinal disease were excluded.

No premedication was given. Upon arrival in the operating theater, the patients were monitored by noninvasive blood pressure monitoring (MDE ESCORT, Medical Data Electronics, Arleta, CA, USA) and standard lead II ECG. The baseline blood pressure and heart rate (T_0) were recorded after a resting period of 5 min, and preoxygenation was subsequently given. One minute after baseline blood pressure was recorded (T_1), either nicardipine or lidocaine was administered intravenously in a double-blind fashion. After another minute, anesthesia was induced by intravenous thiopentone 5 mg·kg^{-1} followed by succinylcholine 1.5 mg·kg^{-1}. Direct laryngoscopy and tracheal intubation was initiated 1 min after administration of thiopentone. Blood pressure (systolic blood pressure, diastolic blood pressure, and mean blood pressure) and heart rate were recorded every 1 min by other independent anesthesiologist until 4 min after intubation (T_8). The study protocol is shown in Fig. 1.

Each intubation was performed by an MD anesthesiologist and was accomplished within 20 s. No patients received topical lidocaine before placement of the tracheal tube. After tracheal intubation, ventilation was controlled with 66% nitrous oxide in oxygen and 0.5% halothane. The study was then completed 4 min after intubation, and the patient received whatever anesthetic agents were deemed appropriate for the procedure. The occurrence of any dysrhythmia was also noted. The rate-pressure product was calculated by multiplying the systolic blood pressure by the heart rate.

Statistical analysis was performed by repeated-measures analysis of variance, Student's t test was used for continuous data and the chi-squared test (Fisher's exact test when appropriate) for categorical data; 95% confidence intervals were calculated when appropriate. $P < 0.05$ was considered statistically significant.

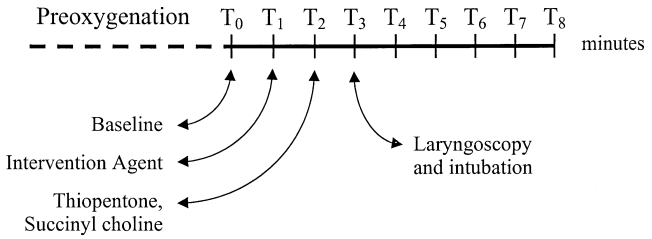

Fig. 1. Time line describing the intervention and data collection points during the study

Table 1. Demographic characteristics of study patients

Characteristic	Nicardipine group	Lidocaine group
No. of patients	30	30
Sex (F/M)	25:5	22:8
Age (yr)		
Mean (SD)	36.5 (10.3)	40.3 (10.3)
Range	16–54	25–59
Weight (kg)		
Mean (SD)	56.5 (8.8)	55.6 (10.6)
Range	40–80	40–79

Results

The demographic characteristics of the patients were comparable in both groups (Table 1). The blood pressure (systolic blood pressure, mean blood pressure, and diastolic blood pressure), heart rate, and rate-pressure product are given as means (SD) (Table 2). The baseline values of systolic blood pressure, mean blood pressure, diastolic blood pressure, heart rate, and rate-pressure product were comparable in both groups.

After the administration of either drugs diastolic blood pressure, mean blood pressure, and heart rate were significantly different between the nicardipine and lidocaine groups ($P < 0.01$, $P = 0.03$, $P < 0.001$, respectively). Systolic blood pressue and rate-pressure product between groups were not significantly different.

The maximal changes in blood pressure and heart rate occured 1 min after laryngoscopy was started. The mean differences in diastolic blood pressure, mean blood pressure, heart rate, and rate-pressure product at baseline (T_0) and 1 min after laryngoscopy was started (T_4) were significantly different between groups; [P = 0.01, 95% CI (−17.311, −1.667); P = 0.01, 95% CI (−17.306, −2.494); $P < 0.001$, 95% CI (13.494, 33.039); and P = 0.01, 95% CI (440.5, 4437.6), respectively, as shown in Fig. 2].

There was one case of occasional premature ventricular contraction (PVC) during laryngoscopy and intubation in the lidocaine group, which spontaneously disappeared within few minutes. Other adverse effects,

Table 2. Mean (SD), systolic blood pressure (sBP), diastolic blood pressure (dBP), mean blood pressure (mBP), heart rate (HR), and rate-pressure product (RPP) in nicardipine and lidocaine groups from 0 (t_0) to 8 (t_8) minutes

Measurement/group	T_0	T_1	T_2	T_3	T_4	T_5	T_6	T_7	T_8
sBP (mmHg)									
Nicardipine	126.6	123.5	114.2	128.7	142.6	136.3	126.5	121.2	118.9
	(15.2)	(14.6)	(18.1)	(25.2)	(20.8)	(21.5)	(17.2)	(18.5)	(16.7)
Lidocaine	126.1	123.3	122.4	149.1	150.8	138.5	129.2	121.3	155.2
	(12.7)	(11.3)	(11.4)	(23.5)	(22.8)	(24.2)	(21.8)	(18.7)	(15.2)
mBP (mmHg)									
Nicardipine	93.3	89.7	83.4	100.3	106.7	100.5	94.0	90.0	88.0
	(12.8)	(9.48)	(16.4)	(18.9)	(15.2)	(16.1)	(12.6)	(14.8)	(12.7)
Lidocaine	93.9	92.8	96.0	117.9	106.8	106.8	98.8	92.0	86.7
	(9.0)	(8.3)	(10.7)	(17.4)	(17.5)	(19.5)	(18.3)	(16.5)	(13.6)
dBP (mmHg)									
Nicardipine	76.7	72.8	68.0	86.1	88.6	82.6	77.8	74.4	72.5
	(12.9)	(9.1)	(17.3)	(17.2)	(13.3)	(14.1)	(11.3)	(13.7)	(11.6)
Lidocaine	77.8	77.6	82.8	102.3	99.8	90.9	83.5	77.3	72.5
	(8.5)	(9.1)	(11.4)	(16.1)	(16.0)	(18.5)	(17.5)	(16.7)	(13.5)
HR (beats min^{-1})									
Nicardipine	79.9	89.9	105.2	117.4	120.3	115.0	107.6	101.9	99.2
	(15.0)	(26.8)	(19.4)	(15.9)	(15.9)	(15.6)	(14.6)	(13.5)	(12.9)
Lidocaine	80.8	82.1	93.0	96.8	97.9	94.9	90.6	87.8	84.8
	(17.8)	(18.5)	(23.7)	(17.6)	(15.8)	(15.5)	(16.6)	(15.1)	(13.6)
RPP ($mmHg \cdot min^{-1}$)									
Nicardipine	10 236.8	11 276.3	12 181.9	15 331.6	17 284.4	15 870.1	13 781.2	12 530.2	11 945.7
	(2 761.0)	(4 052.3)	(3 598.4)	(4 236.6)	(3 755.1)	(4 059.4)	(3 454.5)	(3 429.4)	(3 057.8)
Lidocaine	10 250.2	10 214.0	11 432.0	14 601.6	14 858.8	13 261.2	11 834.4	10 736.8	9 807.5
	(2 688.7)	(2 842.8)	(3 298.2)	(4 153.6)	(3 658.5)	(3 728.3)	(3 397.7)	(2 805.9)	(2 221.5)

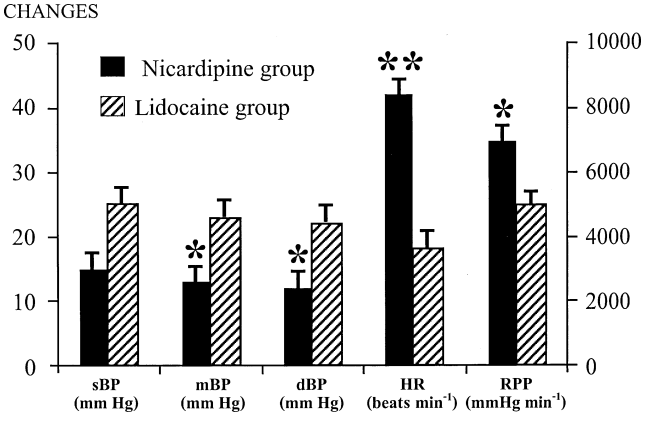

Fig. 2. Comparision of changes in systolic blood pressure (sBP), mean blood pressure (mBP), diastolic blood pressure (dBP), heart rate (HR), and rate-pressure product (RPP) in nicardipine and lidocaine groups. Data represent changes between baseline values (T_0) and 1 min after starting laryngoscopy (T_4). $^*P = 0.01$, $^{**}P = <0.001$. Bars represent SEM

such as bradycardia (heart rate $< 60\,min^{-1}$), hypertension (diastolic blood pressure > 110 mmHg), and rate-pressure product greater than 20 000 $mmHg \cdot min^{-1}$ did not differ significantly between groups (Table 3). No ST segment depression was noted in either group.

Discussion

Increases in blood pressure and heart rate are predictable responses to direct laryngoscopy and tracheal intubation after induction of anesthesia with barbiturate followed by succinylcholine. Typically blood pressure begins to increase after about 15 s of laryngoscopy and becomes maximal after 30 to 45 s of direct laryngoscopy [1]. The mechanism of cardiovascular response to intubation is assumed to be a reflex sympathetic reaction to the mechanical stimulation of the larynx and trachea. Significant elevations in serum levels of epinephrine and norepinephrine following laryngoscopy with and without tracheal intubation have been demonstrated [16–18].

A variety of anesthetic techniques and drugs are available to control the hemodynamic response to

Table 3. Adverse effects during laryngoscopy and intubation

Effect	No. of patients		*P* value
	Nicardipine	Lidocaine	
Premature ventricular contraction	1	0	1
Bradycardia (HR $< 60\,min^{-1}$)	2	6	0.2
Hypertension (dBP > 110 mmHg)	3	9	0.1
RPP > 20000 mmHg·min^{-1}	5	4	1

laryngoscopy and intubation. The method or drug of choice depends on many factors, including the urgency and length of surgery, choice of anesthetic technique, route of administration, medical condition of the patient, and individual preference, but the results are inconclusive [1–3,7–10,19,20]. Since the early 1960s, lidocaine has been focused on blunting the cardiovascular response to intubation, diminishing cough reflexes, dysrhythmia, and rises of intracranial and intraocular pressure [10]. Abou-Madi et al. recommended 1.5 mg·kg^{-1} of lidocaine given intravenously for intubation prophylaxis [21]. Kyokong et al. showed that 1.5 mg·kg^{-1} lidocaine administered intravenously 2 min before intubation was effective in attenuation of the cardiovascular response to laryngoscopy and intubation [10]. Nicardipine is the first intravenously administered dihydropyridine calcium channel blocker. Its primary physiologic actions include vasodilatation, with limited effect on the inotropic and dromotropic functions of the myocardium [12]. It differs from other calcium antagonists with respect to consistent augmentation of coronary blood flow [14]. This property makes nicardipine a potentially attractive drug for preintubation prophylaxis.

Our study compared the efficacy of nicardipine 30 μg·kg^{-1} and lidocaine 1.5 mg·kg^{-1} administered intravenously 2 min before laryngoscopy and intubation for controlling hemodynamic responses. We found that diastolic blood pressure and mean blood pressure were significantly lower but heart rate was significantly higher in the nicardipine group. We did not compare both groups with placebo or control because it had already been shown that either nicardipine or lidocaine could attenuate cardiovascular responses during laryngoscopy and intubation [11,15]. The increase in heart rate in the nicardipine group was caused by reflex sympathetic cardiac compensation induced by peripheral vasodilatation [13]. Cheung et al. showed that blood pressure declined rapidly and reached a nadir 2 min after intravenous injection of nicardipine with mild tachycardia [22]. Because not all statistically significant differences are clinically significant, confidence intervals can address both clinical and statistical significances [23–27]. Despite the statistically significant differences in mean blood pressure, diastolic blood pressure, heart rate, and rate-pressure product ($P = 0.01$, $P = 0.01$, $P < 0.001$, and $P = 0.01$, respectively), the 95% confidence intervals of the mean differences in mean blood pressure, diastolic blood pressure, and rate-pressure product were (−17.311, −1.667), (−17.306, −2.494), and (440.53, 4437.63), which were clinically inconclusive. The 95% confidence interval of the mean difference in heart rate was (13.394, 33.039), which was considered clinically significant. In common with other calcium channel blockers, such as verapamil and diltiazem, nicardipine failed to prevent tachycardia caused by reflex sympathetic cardiac compensation induced by peripheral vasodilatation [5,6].

Although the degree of increase in heart rate was higher in the nicardipine group, the numbers of patients whose rate-pressure product was greater than 20000 mmHg·mm^{-1} were not significantly different. Rate-pressure product greater than 20000 mmHg·min^{-1} has been shown to correlate with angina and myocardial ischemia [28–30]. However, Rao et al. showed that patients with previous myocardial infarction who had intraoperative hypertension and developed tachycardia or hypotension develop a higher incidence of reinfarction [31]. Slogoff and Keats also showed that tachycardia (heart rate $\geq 110\,min^{-1}$) was significantly related to intraoperative ischemia in patients undergoing coronary artery bypass grafting [32]. Therefore, the use of nicardipine for blunting hemodynamic responses should be avoided in patients with ischemic heart disease. In this study there were few minor adverse effects, such as bradycardia and hypertension (diastolic blood pressure > 110 mmHg), and they were not significantly different between the groups. The onset of action of nicardipine is rapid, and its duration is fairly short; the maximum effect is evident approximately 1 min after intubation. In conclusion, nicardipine appears to be an alternative to lidocaine for attenuation of circulatory responses to laryngoscopy and tracheal intubation, except in patients with ischemic heart disease.

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