Comparison of Nicardipine Versus Esmolol in Attenuating the Hemodynamic Responses to Anesthesia Emergence and Extubation

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Objective: **The purpose of this study was to compare the effectiveness of intravenous (IV) nicardipine versus esmolol in controlling heart rate (HR) and blood pressure (BP) responses to emergence and extubation.**

Design: **Prospective, randomized, double blind.**

Setting: **University hospital, single institution.**

Participants: **Twenty-two American Society of Anesthesiologists physical class 1 to 3 adult inpatients scheduled for general anesthesia.**

Interventions: **General endotracheal anesthesia with oxygen/isoflurane and muscle relaxation. At end of surgery, with at least 2 twitches by nerve stimulator and end-tidal isoflurane <0.4%, muscle relaxant reversal was accomplished with neostigmine and glycopyrrolate. Two minutes postreversal, the IV study drug nicardipine, 0.03 mg/kg, or esmolol, 1.5 mg/kg, was administered. HR and BP were measured every minute up to 10 minutes and at minute 15 postreversal.**

Measurements and Main Results: **There were no significant differences between groups in age, weight, gender, American Society of Anesthesiologists physical class or preoperative hemodynamics (HR, BP, mean arterial pressure [MAP]). Compared with nicardipine, 0.03 mg/kg IV, esmolol, 1.5 mg/kg IV, significantly ($p < 0.05$) attenuated HR more than nicardipine for the 15-minute time period poststudy drug. Compared with esmolol, nicardipine was significantly ($p < 0.05$) more effective in controlling MAP and systolic BP for the 1- to 3-minute and diastolic BP for the 1- to 2-minute time periods poststudy drug. There were no episodes of hypotension or adverse events.**

Conclusions: **Although esmolol, 1.5 mg/kg, IV was more effective than nicardipine, 0.03 mg/kg, IV for attenuating the HR response to extubation, nicardipine was more effective in controlling the BP response.**

KEY WORDS: calcium channel blocker, nicardipine, β-blocker, esmolol, hemodynamics, heart rate, blood pressure, mean arterial pressure, emergence, extubation

CONTROL OF THE HEART RATE (HR) and blood pressure (BP) response to endotracheal extubation and emergence from anesthesia are essential to avoid an adverse event and ensure a favorable postoperative outcome, especially in susceptible patients with preexisting cardiac or cerebrovascular disease.[1] A large amount of research has addressed the hemodynamic problems associated with anesthesia induction and intubation. Less research has been conducted on the hemodynamic problems associated with emergence and extubation and the medications necessary to prevent these problems.

To protect the patient from potentially negative outcomes resulting from the effects of anesthesia induction, laryngoscopy, intubation, emergence, and extubation, esmolol[2,3] and nicardipine[4-6] have been found to attenuate the increased hemodynamic responses. Esmolol is an ultra–short-acting, selective, β_1-blocker with a rapid onset that produces a decrease primarily in HR and secondarily in BP. An optimal intravenous (IV) esmolol dose for use during anesthesia induction (laryngoscopy and intubation) and emergence (extubation) has been previously determined to be 1.5 mg/kg.[2,3] Nicardipine is a short-acting calcium channel blocker that has been found useful to control the BP response during intubation, intraoperatively, and during the time of emergence and extubation.[4-6] A previous study by Kovac et al[6] determined that nicardipine, 0.03 mg/kg, IV, was a more effective and optimal dose compared with nicardipine, 0.015 mg/kg, for attenuating the BP response to emergence and extubation. A direct double-blind, prospective comparison of nicardipine versus esmolol during emergence and extubation has not been previously reported.

The purpose of the present study was to compare nicardipine, 0.03 mg/kg, with esmolol, 1.5 mg/kg, to determine their effect on the control of the hemodynamic response (HR, systolic BP, diastolic BP, and mean arterial pressure [MAP]) in patients during extubation and emergence from general endotracheal anesthesia.

METHODS

After institutional review board approval and written informed consent, 22 adult male and female inpatients scheduled to undergo elective surgery under general endotracheal anesthesia were enrolled in this double-blind, prospective, randomized study. Inclusion criteria included patients greater than 18 and less than 80 years of age, American Society of Anesthesiologists physical class 1 to 3, and scheduled for general endotracheal anesthesia with a muscle relaxant (succinylcholine and/or vecuronium). Exclusion criteria included patients who were ASA physical class 4 or 5, had an atrioventricular conduction block greater than first degree, and history of drug allergy or known sensitivity to or presently taking β-blocking or calcium-channel-blocking drugs. Additional exclusion criteria were history of asthma, bronchospasm, chronic obstructive pulmonary disease, coronary artery disease, essential hypertension, diabetes, body mass index >33, HR <60 beats/min, systolic BP <100 mmHg, or diastolic BP <50 mmHg 2 minutes after muscle relaxant reversal.

Patients were premedicated with midazolam, 1 to 2 mg IV, after peripheral catheter placement. After preoxygenation with 100% oxygen for 5 minutes, the trachea was intubated after administration of thiopental, 4 mg/kg, or propofol, 2 mg/kg, and fentanyl, 1 μg/kg, plus succinylcholine, 1.5 mg/kg, or vecuronium, 0.1 mg/kg. Anesthesia was maintained with an end-tidal isoflurane concentration of 0.4% to 2.0%, 50% nitrous oxide in oxygen, fentanyl, 2 to 5 μg/kg, and intermittent IV boluses of vecuronium, 0.02 mg/kg, given as needed to keep the train-of-four at 1 to 2 twitches. Heart rate was measured by a standard 5-lead electrocardiogram, BP, and MAP by noninvasive automatic BP cuff, end-tidal carbon dioxide by capnograph, oxygen saturation by pulse oximeter, and train-of-four muscle relaxation by peripheral twitch

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Table 1. Demographic Variables

	Group 1: Nicardipine, 0.03 mg/kg	Group 2: Esmolol, 1.5 mg/kg
n	11	11
Age (y)	42 ± 4.15	38 ± 4.87
ASA classification		
ASA 1	7	7
ASA 2	2	3
ASA 3	2	1
Sex		
Male	7	3
Female	4	8
Weight (kg)	83 ± 5.38	75 ± 4.37
Preoperative vital signs		
SBP (mmHg)	140 ± 6.55	133 ± 7.44
DBP (mmHg)	83 ± 3.83	76 ± 3.04
MAP (mmHg)	101 ± 4.11	96 ± 3.48
HR (bpm)	77 ± 5.06	83 ± 2.28

NOTE. Values are expressed as mean ± standard error of the mean.
Abbreviations: SPB, systolic blood pressure; DBP, diastolic blood pressure.

monitor at the abductor pollicus brevis. HR and BP were measured every 5 minutes during surgery per routine anesthesia protocol and maintained between 80% and 120% of the preoperative HR and BP baseline values by titration of isoflurane as needed. At the end of surgery, isoflurane and nitrous oxide were discontinued and muscle paralysis evaluated by peripheral nerve stimulator. In the presence of at least 2 twitches and an isoflurane end-tidal concentration of less than 0.4%, muscle relaxant reversal with IV neostigmine, 0.05 mg/kg, and glycopyrrolate, 0.01 mg/kg, was instituted.

The esmolol and nicardipine study drugs were prepared and administered in a double-blind manner. Esmolol was provided as a 10-mg/mL solution in a 10-mL vial. The esmolol dose was calculated at 1.5 mg/kg, and this dose was further diluted with normal saline to a 20-mL total volume. Nicardipine was provided as a 2.5-mg/mL solution in a 10-mL vial. The nicardipine dose was calculated at 0.03 mg/kg, and this dose was further diluted with normal saline to a 20-mL total volume. Study patients were assigned to 1 of 2 groups by randomly drawing numbers from a hat. Study samples were prepared by an individual not involved with the study and were labeled group A or B, with the group study letter and study patient numbers to ensure a blinded study. Group A (n = 11) received esmolol, 1.5 mg/kg, and group B (n = 11) received nicardipine, 0.03 mg/kg. Baseline vital signs (HR and BP) were determined at 1 minute post–muscle relaxant reversal. At 2 minutes postreversal, which was defined as time 0, either the esmolol or nicardipine study drug was administered. After study drug administration, HR and BP measurements were taken every minute for up to 10 minutes and at 15 minutes. Comparisons were made between groups and to baseline HR and BP values. Data were adjusted for baseline (defined as percent [%] change from baseline) mean values. The mean values of the baseline HR and BP were the main reference points for further vital sign measurements. Patients were extubated after the end-tidal isoflurane concentration was <0.3% and extubation criteria defined as sustained tetanus >5 seconds, respiratory rate >12 breaths per minute, positive head lift, hand grip, and eyes following on command were met. A Student unpaired *t* test and chi-square test were used to measure demographic differences between groups. Vital sign data were analyzed by using analysis of covariance for repeated measures. Newman-Keuls multiple comparison tests were applied for pair-wise comparisons. A $p < 0.05$ value was considered statistically significant.

RESULTS

Twelve women and 10 men, ASA physical class 1 to 3, were evaluated, ranging in age from 44 to 52 years, undergoing general endotracheal anesthesia for a variety of inpatient surgical procedures (orthopedic, gynecologic, urologic, and general surgery) were included in the study. Demographic data are listed in Table 1. There were no significant differences between groups regarding age, weight, ASA physical class, or preoperative hemodynamic vital signs. There were no differences between groups in regard to procedure duration or time from end of surgery to tracheal extubation (Table 2).

Figure 1 shows the differences in the mean HR adjusted-for-baseline (% change from baseline) values between the 2 study groups. Heart rate increased significantly ($p < 0.05$) in the nicardipine group 2 minutes after completion of the surgical procedure and 1 minute postadministration of the neuromuscular reversal agent. Esmolol significantly ($p < 0.05$) attenuated HR more than nicardipine at all measured time intervals (Fig 1). Compared with esmolol, nicardipine was significantly more effective in attenuating systolic BP (Fig 2) at minutes 1 to 3 poststudy drug and diastolic BP and MAP (Figs 3 and 4, respectively) at minutes 1 and 2 poststudy drug. Although statistical differences were noted between the 2 drugs, the main clinical difference observed was HR attenuation with esmolol and BP attenuation with nicardipine. No adverse effects or side effects were noted with either nicardipine or esmolol.

DISCUSSION

During induction, laryngoscopy, intubation, and at the time of extubation and emergence, the human body's normal response to stress is often exhibited as tachycardia and hypertension, with HR and BP increases of greater than 20%.[1,7] Hypertensive patients, whether treated or untreated, exhibit greater increases in BP (compared with baseline preinduction values) during endotracheal intubation, emergence, and extubation compared with normotensive patients.[1,8] Stone et al[9] determined that HR and BP increased significantly during emergence and endotracheal extubation and paralleled the hemodynamic increases associated with intubation.

For patients at risk and who may have untreated or poorly controlled hypertension at the time of emergence and extubation, the stresses that occur during extubation and emergence may cause an even more exaggerated BP response than would be expected with normotensive patients. Such increases in BP could result in cardiac decompensation, myocardial ischemia, pulmonary edema, or cerebral hemorrhage in susceptible patients. Control of the tachycardic and hypertensive response is essential to prevent an adverse event.

Table 2. Procedure Duration

	Group 1: Nicardipine, 0.03 mg/kg	Group 2: Esmolol, 1.5 mg/kg
Procedure duration (min)	104 ± 16.96	92 ± 13.23
Time from procedure completion to tracheal extubation (min)	6.6 ± 0.87	5.9 ± 0.73

NOTE. Values are expressed as mean ± standard error of the mean.