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Original contribution

The optimal dose of esmolol and nicardipine for maintaining cardiovascular stability during rapid-sequence induction

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Abstract

Study Objective: To determine the optimal dose of esmolol in combination with nicardipine in effectively blocking undesirable cardiovascular responses during rapid-sequence induction.

Design: Prospective, randomized clinical comparison study.

Setting: Operating room of a university hospital.

Patients: 200 ASA physical status 1 and 2 patients requiring general anesthesia with endotracheal tube placement.

Interventions: Patients were randomly allocated into one of 4 groups: Group E0 (no esmolol; control), Group E0.25 (esmolol 0.25 mg/kg), Group E0.5 (esmolol 0.5 mg/kg), and Group E1.0 (esmolol 1.0 mg/kg). All patients received 20 μg/kg of nicardipine, and esmolol was then given according to group allocation. Ninety seconds later, thiopental sodium 5 mg/kg and succinylcholine 1.0 mg/kg were injected. Endotracheal intubation was performed 60 seconds after injection of the anesthetic agents.

Measurements: Systolic (SBP), diastolic (DBP), and mean arterial (MAP) pressures; heart rate (HR), and rate-pressure product (RPP) were measured 30 seconds before and after intubation, and at 1, 3, 5, and 10 minutes after intubation. Rate changes using baseline values as the standard [rate changes = measured value/baseline value × 100 (%)] were calculated.

Main Results: Significant attenuations in SBP, MAP, HR, and RPP after intubation were noted in the experimental groups as compared with the control group ($P < 0.05$). Rate changes in HR in Groups E0.5 and E1.0 were significantly lower than those in Group E0.25 immediately and one minute after intubation ($P < 0.05$). No difference in rate changes in HR were noted between the E0.5 and E1.0 groups.

Conclusions: The combination of nicardipine 20 μg/kg and esmolol 0.5 mg/kg most effectively attenuates the cardiovascular responses during rapid-sequence induction.

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1. Introduction

Control of the heart rate (HR) and blood pressure (BP) response to endotracheal intubation is essential to prevent adverse cardiovascular outcomes. Rapid-sequence induction is unavoidable in patients with intestinal obstruction, ascites, hiatal hernia, and gastroesophageal reflux disease; and in those with an insufficient presurgical fasting period. Nicardipine and esmolol are considered appropriate for control of hemodynamics during rapid-sequence induction due to their fast onset and short duration.

Nicardipine is an antihypertensive agent with high vascular selectivity and no discernible effect on ventricular contractility [1]. However, reflex tachycardia in response to the vasodilation induced by nicardipine may occur [1]. Esmolol primarily blocks tachycardia and decreases BP. Esmolol may be used efficiently to block the tachycardia induced by nicardipine [2].

The purpose of this study was to determine the optimal dosage of esmolol that may be effectively administered in combination with nicardipine during rapid-sequence induction.

2. Materials and methods

This study was approved by the Institutional Review Board of Catholic University Seoul-Saint Mary's Hospital, and informed consent was obtained from all study subjects. This study was conducted in 200 adult, ASA physical status 1 and 2 patients scheduled to undergo elective noncardiac surgery between October 2008 and April 2009. Patients with hypertension, arrhythmia, myocardial ischemia, hyperkalemia, or allergy to the study drugs were excluded from the study.

On arrival at the preanesthetic care unit, patients were assigned randomly to one of 4 groups by a computer-generated randomization table: Group E0 (esmolol 0 mg/kg), Group E0.25 (esmolol 0.25 mg/kg), Group E0.5 (esmolol 0.5 mg/kg), and Group E1.0 (esmolol 1.0 mg/kg), based on estimated ideal body weight. Group E0 served as the control group. Other than antibiotics, no drugs were used for premedication. Nurses who did not participate in this study prepared the study drugs, all of which were diluted to 10 mL.

In the operating room, routine monitors were applied, including a blood pressure cuff, electrocardiogram, pulse oximeter, and capnogram. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), HR, and rate-pressure product (RPP) were measured to determine baseline values. For volume loading, a rapid infusion of lactated Ringer's solution (1.0 mL/kg/min) was given during the data collection period. After adequate preoxygenation, patients received intravenous (IV) nicardipine 20 μg/kg immediately followed by esmolol, according to group allocation. All test drugs were administered as rapid injections. After 90 seconds, thiopental sodium 5 mg/kg and succinylcholine chloride 1.0 mg/kg were administered for induction of anesthesia, with the dose given based on estimated ideal body weight. Endotracheal intubation by laryngoscopy was performed 60 seconds after the administration of succinylcholine. All endotracheal intubations were performed with the Sellick maneuver by two attending anesthesiologists who were not associated with this study. If the first attempt at intubation failed or the laryngoscopic procedure took longer than 20 seconds, the case was excluded from the study. The hemodynamic data were recorded 30 seconds before and after intubation and at 1, 3, 5, and 10 minutes after intubation. The anesthesiologists who participated in the intubation and recording of data were unaware of patients' group allocation. Anesthesia was maintained with sevoflurane 1.5% (inspired concentration) in 60% nitrous oxide/oxygen during the period of data collection. Mechanical ventilation was regulated to maintain end-tidal CO_2 ($ETCO_2$) at 35 to 40 mmHg. Drugs that could have influenced the cardiovascular response during endotracheal intubation, eg, lidocaine, opioids, and vasodilators, were not used during the study period. For cases with HR < 55 beats per minute (bpm), atropine 0.25-0.5 mg IV was given and these patients were excluded from the study. Likewise, for cases with SBP < 80 mmHg, ephedrine 5 mg IV was administered and these patients were excluded from the study.

2.1. Statistical analysis

A power analysis was performed on the basis of $\Delta(\mu\text{-}\mu' / \delta) = 0.6$ (where $\mu\text{-}\mu'$ = difference in mean and δ = SD), $\alpha = 0.05$, and $\beta = 0.2$ (power of 80%), which determined that a sample size of 45 patients per group was adequate to detect a significant difference in peak HR values after tracheal intubation. To compensate for potential dropouts, we enrolled 50 patients in each group.

For data obtained at each time point, the rate of change was calculated (rate change = measured value/baseline value × 100 (%) and presented as the average of the rate change ± standard deviation. Height, weight, age and baseline hemodynamic values were compared by one-way analysis of variance (ANOVA). Changes in BP, HR, and RPP within each group were analyzed by repeated measures ANOVA. If a significant difference was detected, post hoc analysis was performed by Bonferroni's or Tukey's correction. Chi-square tests or Fisher's exact tests were used for analysis of nonparametric data. SPSS software for Windows (version 15.0; SPSS Inc., Chicago, IL, USA) was used for the analysis. *P*-values < 0.05 were considered statistically significant.

3. Results

Among the 200 patients who participated in this study, 4 patients were excluded for various reasons. Laryngoscopy