Does a single dose of intravenous nicardipine or nimodipine affect the bispectral index following rapid sequence intubation?

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Background: Theoretically, L-type calcium channel blockers could modulate anesthetic effects. Nicardipine does not affect the bispectral index (BIS), but nimodipine, which can penetrate the blood-brain barrier, has not been studied. The aim of this study was to evaluate whether a single dose of intravenous nicardipine or nimodipine could affect BIS following rapid sequence intubation.

Methods: This study was done in a double-blind, randomized fashion. Anesthesia was induced with fentanyl 2 μg/kg, thiopental sodium 5 mg/kg, and 100% oxygen. After loss of consciousness, patients received rocuronium 1.0 mg/kg and either a bolus of 20 μg/kg nicardipine, nimodipine, or a comparable volume of normal saline (n = 20). Intubation was performed 1 min after study drug administration. BIS, mean blood pressure (MBP), and heart rate (HR) were measured before anesthetic induction, after loss of consciousness, before intubation, during intubation, and 1, 2 and 5 min after intubation.

Results: BIS dropped rapidly after induction but increased to 60 before intubation in all groups irrespective of study drug. In nimodipine, the increase in BIS during intubation was not significant compared to pre-intubation, in contrast to the other two groups, but there was no difference in BIS during intubation. HR significantly increased, but MBP just rose to pre-induction values after intubation in nicardipine and nimodipine groups. BIS, MBP, and HR following intubation increased in control group.

Conclusions: A single dose of intravenous nicardipine or nimodipine could attenuate blood pressure increases but not affect BIS increases in rapid sequence intubation. (Korean J Anesthesiol 2010; 59: 256-259)

Key Words: BIS, Intubation, Nicardipine, Nimodipine.
Introduction

Theoretically, L-type calcium channel blockers (CCB) could influence anesthetic potency through modulating intracellular messenger function and post synaptic neuronal excitability, affecting secretion of neurotransmitters, or indirectly altering hemodynamics. L-type calcium channels exist in sensory neurons in the spinal cord and the brain [1,2]. L-type CCB potentiate the action of sedatives [3], opioids [4], and anesthetics [5] and several anesthetics act on L-currents in neurons [6-8]. However, CCB activity on anesthesia is still controversial [9,10]. If CCB is administered via a peripheral intravenous route, it needs to cross the blood-brain barrier (BBB) to show anesthetic effects. Nicardipine weakly crosses the BBB, whereas nimodipine crosses better [11].

Intubation causes a peripheral nociceptive response that can induce central arousal [12]. Endotracheal intubation can increase the bispectral index (BIS) and change hemodynamics [12,13]. We compared BIS and hemodynamic changes for nicardipine and nimodipine, which cross the BBB differently, after rapid sequence endotracheal intubation.

Materials and Methods

This study was approved by the Institutional Review Board of our hospital, and written informed consent was obtained from each patient. We enrolled ASA physical status I patients who were scheduled for elective surgery under general anesthesia. Patients with a history of hypertension, diabetes mellitus, body weight >130% of ideal body weight, cardiovascular or cerebrovascular disease, and those receiving medications that affect cardiovascular and psychological function were excluded. The age range was from 18–60 years. Patients were randomly allocated into 3 groups using a computer-generated sequence (n = 20, each).

No premedication was administered. All patients were monitored with noninvasive blood pressure, electrocardiogram, temperature, and peripheral oxygen saturation. BIS was monitored using an Aspect A-1000 EEG monitor, version 3.12 (Aspect Medical Systems, Natick, USA). Baseline values of BIS and vital signs were recorded before induction of anesthesia. Rapid sequence intubation was designed to increase BIS in the control group. Under monitoring, intravenous fentanyl 2 μg/kg was given and anesthesia was induced with thiopental sodium 5 mg/kg and 100% oxygen. After loss of consciousness, patients received rocuronium 1.0 mg/kg and at the same time either a bolus of nicardipine 20 μg/kg, nimodipine 20 μg/kg, or a comparable volume of normal saline. One minute after study drug administration, the trachea was intubated with a direct laryngoscope by a second-year anesthesia resident. Only one attempt was allowed for tracheal intubation. Intubation was accomplished within 30 sec in all cases. After intubation, ventilation was controlled with 1 vol% sevoflurane in 100% oxygen for 5 min. End-tidal carbon dioxide concentration was maintained between 35–40 mmHg throughout the study. Mean blood pressure (MBP), heart rate (HR), and BIS value were recorded before induction of anesthesia (B0), after loss of consciousness (B1), before intubation, during intubation (L0), 1, 2 and 5 min after intubation (L1, 2, and L5). We allocated 16 patients to each group to detect a 5-point increase in BIS after intubation, with \( \alpha = 0.05 \) and \( \beta = 0.2 \) [14]. To compensate for drop out, we targeted 20 patients in each group. Data are presented as mean ± SD. SPSS version 12.5 (SPSS Inc, Chicago, IL) was used for analysis.

Statistical analysis was performed using the chi-square test or one-way analysis of variance followed by the Tukey test. One-way analysis of variance for repeated measures followed by multiple comparisons was performed for time-dependent variables. \( P < 0.05 \) was considered statistically significant.

Results

A total of 63 patients were included in the study. Two patients in the nicardipine group and one patient in the control group were excluded from the study due to difficult intubation. No differences were observed in demographic data, baseline hemodynamics, and BIS values before induction of anesthesia (Table 1).

BIS values rapidly fell after induction of anesthesia (B1) and then increased up to 60 just before intubation in all groups. Nicardipine or nimodipine injection did not affect BIS values 1 min after drug injection. BIS values significantly increased by 7-8 after intubation in controls compared to baseline (B2) (\( P < 0.05 \), Table 2). Nicardipine injection did not block the increase in BIS following intubation. In the nimodipine group, the increase in BIS during intubation (L0) was not significantly different than baseline (B2), in contrast to the other two groups. However, there was no difference in BIS during intubation (L0) in any group (\( P = 0.09 \) vs. control) (Table 2).

MBP fell before intubration in all groups (B2), with larger

### Table 1. Characteristics of Patients

|                      | Control group  | Nicardipine group | Nimodipine group |
|----------------------|----------------|-------------------|------------------|
|                      | \( n = 20 \)   | \( n = 20 \)      | \( n = 20 \)     |
| Sex (M/F)            | 9/11           | 7/13              | 8/12             |
| Age (yr)             | 45.1 ± 10.2    | 43.7 ± 9.3        | 43.6 ± 11.0      |
| Weight (kg)          | 57.3 ± 10.7    | 56.5 ± 12.0       | 58.0 ± 13.1      |
| Height (cm)          | 160.1 ± 10.8   | 159.4 ± 10.1      | 161.1 ± 11.4     |

Values are mean ± SD and the number of patients. There were no statistical differences among groups.
changes in the nimodipine group (P < 0.05 compared to controls). Intubation increased MBP in controls, but the MBP at 1 or 2 min after intubation (L1, L2) in nimodipine or nicardipine group was similar to before anesthetic induction (P < 0.05 compared to control group) (Table 3).

HR significantly rose 1 min after intubation and remained elevated in the control group (P < 0.05 compared to pre-induction value). HR rose at 1 min after administration of nicardipine or nimodipine, and remained elevated until 5 min after intubation in the nicardipine or nimodipine group. The nicardipine group showed the highest HR during intubation and 2 min after intubation (L0 and L2) (Table 3).

**Discussion**

Here, a single dose of intravenous nicardipine or nimodipine blocked blood pressure increases after rapid sequence endotracheal intubation, but did not change BIS increases. CCB may modify anesthetic effects. Dihydropyridine CCB and nitrendipine potentiate the anesthetic effects of benzodiazepine, may modify anesthetic effects. Dihydropyridine CCB and Bay K 8644 (an L-type calcium channel activator) reduced the anesthetic potency of midazolam [3]. Verapamil

![Table 2. Changes in Bispectral Index (BIS) in Response to Intubation](image)

Data are presented as mean ± SD (n = 20, each group). L0: during intubation, L1, L2, L5: 1, 2, 5 min after intubation. *P < 0.05 compared to before intubation (B2).

![Table 3. Changes in Mean Blood Pressure (MBP) and Heart Rate (HR) in Response to Intubation](image)

Data are presented as mean ± SD (n = 20, each group). B1: after loss of consciousness, B2: before intubation, L0: during intubation, L1, L2, L5: 1, 2, 5 min after intubation. *P < 0.05 versus before induction. †P < 0.05 compared to control group.
the BIS value did not change in response to intravenous epinephrine, but the BIS 70 value rose after epinephrine treatment [27]. Esmolol can blunt the increase in BIS after endotracheal intubation during sevoflurane anesthesia but not desflurane anesthesia [28], probably via the sympathetic stimulation of desflurane. The same stimulation induces different BIS responses according to the underlying conditions. We evaluated the effects of nicardipine and nimodipine on BIS in rapid sequence intubation, which might increase BIS values. However, nicardipine and nimodipine did not affect pre-intubation BIS values in the range of 57–60.

In conclusion, a single dose of intravenous nicardipine or nimodipine decreased the blood pressure response to endotracheal intubation, but did not affect the BIS increase. These results suggest that a single dose of intravenous nicardipine or nimodipine can blunt the hemodynamic response associated with endotracheal intubation but does not affect anesthetic depth in rapid sequence intubation.

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