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Original contribution

Systemic lidocaine decreases the Bispectral Index in the presence of midazolam, but not its absence☆,☆☆,★

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Abstract

Study Objective: To evaluate the effects of intravenous (IV) lidocaine on the Bispectral Index (BIS) in the presence or absence of midazolam.

Design: Prospective, randomized, double-blinded, placebo-controlled clinical study.

Setting: Operating room of a university hospital.

Patients: 96 ASA physical status 1, 2, and 3 patients undergoing general anesthesia.

Interventions: Patients were assigned to one of 6 treatment groups to receive IV midazolam (0.03 mg/kg) or placebo, followed 5 minutes later by one of three IV preinduction doses of lidocaine: 0.5, 1.0, or 1.5 mg/kg.

Measurements: BIS values were recorded before administration of lidocaine and at 30-second intervals afterwards for three minutes. The primary endpoint was the average BIS level recorded.

Main Results: Baseline BIS values were lower in the midazolam group (94 ± 4 vs. 90 ± 7, $P < 0.001$). There was no significant decrease in BIS values in the placebo group for any of the three lidocaine doses. However, in the midazolam groups, significant decreases in BIS levels versus baseline values were measured.

Conclusion: IV lidocaine decreases BIS in the presence of midazolam, suggesting that the effect of lidocaine on BIS is not direct, but rather results from modulation by midazolam.

1. Introduction

Intraoperative systemic lidocaine shortens postoperative ileus duration and hospital stay [1]. However, systemic lidocaine appears to affect the Bispectral Index (BIS): intravenous (IV) lidocaine administered during propofol or sevoflurane anesthesia reduces anesthetic doses required to

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achieve target BIS values [1,2], and an inadvertently high dose of lidocaine decreased BIS to 0 during sevoflurane anesthesia [3]. Even intrathecal lidocaine leads to sedation and a decrease in BIS. This effect was not related to block height [4]. However, Ozkan-Seyhan *et al* showed that intrathecal bupivacaine may potentiate the effects of intravenous sedation. They reported that a high spinal block (T1-T4) was associated with a faster onset, delayed recovery, and lower doses of propofol sedation compared with a low spinal block (T9-T11) [5]. Nevertheless, it is not clear whether systemic lidocaine potentiates the effects of other anesthetics. Therefore, we studied the interaction between IV lidocaine and BIS in the absence of a general anesthetic. We hypothesized that lidocaine itself may not affect BIS.

If the effect of lidocaine on BIS changes during general anesthesia is indeed indirect, the fact that it occurred with both sevoflurane and propofol suggests that it may potentiate effects of gamma-aminobutyric acid (GABAergic) compounds in general [1,2]. Therefore, we hypothesized that lidocaine would affect BIS in the presence of midazolam. We tested this hypothesis by studying the interaction between IV lidocaine and BIS against a background of a sedative of IV midazolam.

2. Materials and methods

2.1. Study population

University of Virginia Institutional Review Board approval was granted for the trial. A sample size of 96 was determined based on an effect size of 5, standard deviation of 5, with a power of 0.8, based on data from a retrospective chart review.[1] Informed consent was obtained from 97 adult, ASA physical status 1, 2, and 3 patients scheduled to undergo IV induction of general anesthesia. Exclusion criteria included emergency surgery, cardiovascular instability or the presence of an unstable cardiac rhythm, weight greater than 100 kg, concurrent pregnancy, allergy to midazolam or lidocaine, or acute or chronic use of drugs affecting the GABAergic system. Subjects were randomized to receive either IV midazolam (0.03 mg/kg) or IV placebo, followed by one of three lidocaine doses: 0.5 mg/kg, 1.0 mg/kg, or 1.5 mg/kg (Table 1). Hence, 6 groups of 16 subjects were studied.

2.2. Protocol

BIS values were recorded by a study-blinded member of the research staff. The anesthesia provider was unblinded and administered the study drugs. After informed consent was obtained by research staff, the anesthesia provider received a sealed envelope containing the randomized treatment assignment for that subject, and consequently administered a midazolam or placebo premedication, approximately 5 minutes before induction. In the operating room, routine monitors – noninvasive blood pressure, pulse oximeter, and electrocardiogram – were placed. A BIS device (A-2000 XP with BIS Quatro adult sensor; Aspect Medical Systems, Norwood, MA, USA) was also attached to all patients. Baseline BIS values, blood pressure (BP), and heart rate (HR) values were recorded. Subjects were then given the indicated dose of lidocaine as a slow bolus injection through a free-running IV catheter. BIS, BP, and HR values were recorded every 30 seconds for the following three minutes. At the end of three minutes, patients were asked if they had experienced any side effects from the lidocaine (eg, ringing in the ears, metallic taste in mouth, perioral tingling, or numbness). General anesthesia was then induced with propofol. The frequency of marked sedation before propofol and the frequency of obvious discomfort on injection of propofol were also recorded.

Table 1 Group assignment

Group	Premedication	Lidocaine dose (mg/kg)
1	placebo	0.5
2	placebo	1.0
3	placebo	1.5
4	0.03 mg/kg of midazolam	0.5
5	0.03 mg/kg of midazolam	1.0
6	0.03 mg/kg of midazolam	1.5

2.3. Statistical analysis

The mean BIS values recorded during the three minutes after the injection of lidocaine for each subject were compared with baseline using a two-tailed paired t-test. Baseline data from the placebo group and the midazolam group were compared using a two-tailed unpaired t-test. Systolic (SBP) and diastolic (DBP) blood pressure and HR were compared between the midazolam and placebo groups using a two-tailed unpaired t-test. Data are presented as means ± SD unless otherwise indicated.

3. Results

3.1. Study population

Demographic data were comparable between groups (Table 2). There was a significant difference in SBP and DBP, but not HR, between the placebo and midazolam groups before administration of lidocaine.

[1] Groves DS, Malik ZM, Durieux M. Midazolam modulates effects of intravenous lidocaine on bispectral index (BIS) [Abstract]. Anesthesiology 2007;107:A803.