Effect of Esmolol on the Bispectral Index in Patients Undergoing Tracheal Intubation during Induction of Anesthesia

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Abstract

Background: To evaluate the effect of esmolol on bispectral index (BIS) in patients undergoing tracheal intubation during induction of anesthesia, and investigate the mechanism of its inhibiting cardiovascular response to tracheal intubation.

Methods: Forty patients, ASA physical status I or II, aged 20-60 yr, were randomly divided into 2 groups (n=20 each): Control group and Esmolol group. Anesthesia was induced with midazolam 0.1mg/kg, fentanyl 5μg/kg and vecuronium 0.1 mg/kg. Infusion of saline (control group) and esmolol (bolus of 1 mg/kg and then 250μg•kg⁻¹•min⁻¹; esmolol group) was started 1 min before the induction of anesthesia and was continued throughout the study. Mean arterial pressure (MAP), heart rate (HR) and BIS were recorded before esmolol administration (T0), immediately before induction of anesthesia (T1) and tracheal intubation (T2), and every minute after intubation for 3 times (T3, T4, and T5).

Results: There were no significant differences in HR, MAP and BIS between the two groups at the time points of T0, T1, and T2. Compared to T2, HR and MAP significantly increased after tracheal intubation in both groups BIS was between 96 and 99 for all patients at baseline and decreased during the induction of anesthesia. HR, MAP and BIS were significantly lower in esmolol group than that in control after intubation at the time points of T3, T4 and T5 (P<0.05).

Conclusion: Esmolol could suppress BIS increase and inhibit nociceptive response during tracheal intubation; its mechanism may be related to its inhibiting cardiovascular response.

Keywords: Esmolol; Bispectral Index (BIS); Cortisol

Introduction

Esmolol, a short-acting β1-adrenoceptor antagonist, produces attenuation of cardiovascular response to tracheal intubation during induction of anesthesia. Research has shown that esmolol has a certain role in antinociceptive effect, whether its antinociceptive effect related to attenuation of cardiovascular response to tracheal intubation is yet to be further explored, bispectral index (BIS) monitoring can help to evaluate the depth of sedation during induction of anesthesia [1,2]. Compared to the emergence mechanisms, the operating mechanisms of general anesthetics at the induction should be better investigated. The anesthesia-induced loss of consciousness undergoes conditioning of numerous factors that can also influence the BIS analysis and results [3,4]. The purpose of this research is to evaluate the effect of esmolol on bispectral index (BIS) in patients undergoing tracheal intubation during induction of anesthesia, and investigate the relationship between changing BIS values and inhibition of cardiovascular response.

Methods

This study was approved by the Ethics Committee of Guizhou Provincial People's Hospital (Guiyang, China). Written informed consent was obtained from all enrolled parturients. This study was conducted at the Department of Anesthesiology, Guizhou Provincial People's Hospital between December 1, 2015, and December 1, 2017. All patients were ASA physical status I or II, aged 20-60 yr, and weighed 51~65 kg and scheduled for elective surgery were randomly divided into 2 groups (n =20 each): Esmolol group and control group. Exclusion criteria included cardiac disease, metabolic diseases, chronic hypertension, neurological and psychiatric history, routine use of hypnotic medication and β-blocker medication. Electrocardiogram (ECG), blood pressure (BP), the pulse of oxygen saturation (SpO₂), heart rate (HR), mean arterial pressure (MAP) and end-tidal carbon dioxide partial...
Pressure (PETCO₂) were routinely monitored during the operation. A2000XP BIS monitor (Aspect Corporation, USA) was used to monitor BIS. Infusion of saline (control group) and esmolol (bolus of 1 mg/kg and then 250μg·kg⁻¹·min⁻¹ esmolol group) was started 1 min before the induction of anesthesia and was continued throughout the study. After preoxygenation, anesthesia was induced with intravenous injection (I.V.) midazolam 0.1mg/kg, fentanyl 5μg/kg and vecuronium 0.1 mg/kg. Subsequently, they were mechanically ventilated to maintain end-tidal carbon dioxide concentration between 35 ~ 40 mmHg after intubation. Mean arterial pressure (MAP), heart rate (HR) and BIS were recorded before esmolol administration (T0), immediately before induction of anesthesia (T1) and tracheal intubation (T2), and every minute after intubation for 3 times (T3, T4, T5).

Blood samples were collected before esmolol administration and immediately after intubation and preserved at -20 °C for the detection of serum cortisol. Cortisol level were detected by enzyme-linked immunosorbent assay (ELISA) (the kits purchased from Shanghai Boyun Biotechnology Institute).

**Statistical Analysis**

All statistical analyses were performed using SPSS16.0, measurement data was presented as means (SD), the difference in the group was analyzed by paired t-test, the difference between groups was analyzed by one-way analysis of variance (ANOVA), and enumeration data was analyzed by Chi-square test. Differences with \( P \) values of <0.05 were considered significant.

**Results**

No significant differences were found between the esmolol and control groups with respect to age, Height, BMI, ASA Class, and sex ratio (Table 1).

There were no significant differences in HR, MAP and BIS between the two groups at the time points of T0, T1, and T2. Compared to T2, HR and MAP significantly increased after tracheal intubation in both groups; BIS was between 96 and 99 for all patients at baseline and decreased during the induction of anesthesia. HR, MAP and BIS were significantly lower in esmolol group than that in control after intubation at the time points of T3, T4 and T5 (\( P < 0.05 \)) (Figure 1, 2 and 3).

<table>
<thead>
<tr>
<th></th>
<th>Con group (n=20)</th>
<th>Esmol group (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>45.9 (17.5)</td>
<td>48.5 (16.2)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>157.9 (5.2)</td>
<td>158.3 (6.7)</td>
</tr>
<tr>
<td>BMI</td>
<td>22.1 (4.5)</td>
<td>22.0 (3.4)</td>
</tr>
<tr>
<td>ASA Class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>II</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Sex ratio(male/female)</td>
<td>9-Nov</td>
<td>8-Dec</td>
</tr>
</tbody>
</table>

*\( P < 0.01 \) vs. Con group

**Figure 1:** The effect of Esmolol on BIS for patients undergoing oro-tracheal intubation during induction of anesthesia.
In this study, a bolus of esmolol 1 mg/kg before anesthesia induction and followed by an infusion of esmolol 250μg·kg⁻¹·min⁻¹ so as to ensure esmolol blocks β1-adrenergic receptor effectively. The method of anesthesia that was induced with i.v. midazolam 0.1mg/kg, fentanyl 5μg/kg and vecuronium 0.1 mg/kg has little effect on circulation so as to maintain the hemodynamic stabilization. BIS is used to evaluate the change of anesthesia depth in this study because BIS is well related to the dose of midazolam [3].

This study demonstrates that the dose of esmolol that blocks β1-adrenoceptor effectively has no effect on BIS before intubation, but can inhibit the increase of BIS when noxious stimulation such as intubation. The result suggests that antinociceptive effect of esmolol is related to inhibiting cardiovascular response to tracheal intubation.

**Discussion**

In this study, Bolus of esmolol 1 mg/kg before anesthesia induction and followed by an infusion of esmolol 250μg·kg⁻¹·min⁻¹ so as to ensure esmolol block β1-adrenergic receptor effectively. The method of anesthesia that was induced with i.v. midazolam 0.1mg/kg, fentanyl 5μg/kg and vecuronium 0.1 mg/kg has little effect on circulation so as to maintain the hemodynamic stabilization. BIS is used to evaluate the change of anesthesia depth in this study because BIS is well related to the dose of midazolam [3].

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Esmolol had no effects on isoflurane minimum alveolar concentration (MAC) alone, but that MAC was decreased when esmolol was given along with alfentanil, suggesting a possible potentiation of opioid action by esmolol [4,5]. Esmolol can change the intracorporal distribution of opiates and increase its blood concentration [6]. It prompts that the inhibiting effect of Esmolol on cardiovascular response is by enhancing antinociceptive effect of fentanyl [7]. The sedation of fentanyl is so little that esmolol has no effect on BIS before intubation, while Esmolol is helpful to maintain the stable of BIS by potentiate antinociceptive effect of fentanyl which inhibits stress response by suppressing excitability of transmitting pathway and center when intubation [8].

Some studies demonstrate that β-adrenergic receptor resides in different parts of brain stem network system; local administration of β-receptor agonists can activate EEG, while local administration of antagonist will inhibit EEG [9,10]. It prompts β-adrenoceptor antagonist-esmolol has certain central antinociceptive effect.

**Conclusion**

Esmolol could suppress BIS increase and inhibit nociceptive response during tracheal intubation; its mechanism may be related to its inhibiting cardiovascular response.

**References**