

# Evaluation Of The Dose Of Remifentanyl During One Of The Methods Of Short-Term Anesthetic Induction With Antecedent Administration Of Remifentanyl

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## Citation

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## Abstract

**Purpose:** Antecedent administration is a technique used to increase the effect-site concentration (ESC) of remifentanyl during intubation. We evaluated the remifentanyl dose for one of the methods of short-term anesthetic induction with antecedent administration.

**Methods:** This study included 20 patients aged 18–64 years with American Society of Anesthesiologists (ASA) physical status I or II. They were randomly assigned to the following groups: low-dose (LD) group (0.25  $\mu\text{g/kg/min}$ ) and middle-dose (MD) group, (0.5  $\mu\text{g/kg/min}$ ). Intubation was performed 3 min after anesthetic induction by using propofol and rocuronium with antecedent administration of remifentanyl for 2 min. Pulse oximetry oxygen saturation, hemodynamic parameters, and bispectral index (BIS) values were measured, and the ESCs of remifentanyl were calculated.

**Results:** Patient demographics showed no significant differences. None of the patients exhibited oxygen desaturation or experienced a cannot-ventilate situation. Although there were no significant intergroup differences in the degree of decrease in hemodynamic values due to anesthetic induction, the post-intubation hemodynamic and BIS values in the LD group were significantly higher than those in the MD group.

**Conclusion:** We found that administration of remifentanyl at a dose of 0.5  $\mu\text{g/kg/min}$  during anesthetic induction with antecedent administration could blunt the cardiovascular response to intubation and the increase in the BIS values due to intubation without causing any respiratory disorders or worsening suppressing of hemodynamics due to anesthetic induction. Therefore, we suggest that the 0.5  $\mu\text{g/kg/min}$  remifentanyl dose may be better than the 0.25  $\mu\text{g/kg/min}$  dose in this method of short-term anesthetic induction.

## NOTE

Received from the Department of Anesthesiology and Critical Care Medicine, Asahikawa Medical University, Hokkaido, Japan. This study was supported solely from the institutional and/or departmental sources and was presented at the annual meeting of the Japanese society of intravenous anesthesia, at Matsumoto, Japan, on September 26, 2010.

## INTRODUCTION

The remifentanyl dose used in each method of short-term anesthetic induction needs to be evaluated because the recent use of rocuronium has shortened the interval between anesthetic induction and intubation [1]. Therefore, the effect-site concentration (ESC) of remifentanyl should be efficiently increased until intubation. Although antecedent administration of remifentanyl is one of the methods for increasing the concentration of remifentanyl, an extremely

high dose can cause rigidity and an insufficient dose can prevent the ESC increase required during short-term induction [2]. Here, we evaluated the remifentanyl dose for one of the methods of short-term anesthetic induction with antecedent remifentanyl administration.

## MATERIALS AND METHODS

The study was approved and monitored by the Research Ethics Committee of Asahikawa Medical University, and informed consent was obtained from each patient. The study population consisted of 20 patients (age, 20–64 years) who were scheduled to undergo ophthalmologic or otolaryngologic surgery and had American Society of Anesthesiologists (ASA) physical status I or II. Patients with arrhythmias such as atrial fibrillation or disturbance in the conduction system and those receiving  $\beta$ -methyl dopa or clonidine treatment were excluded from this study. The 20

patients were randomly assigned to 2 groups, namely, a low-dose (LD) group (0.25  $\mu\text{g/kg/min}$ ) and a middle-dose (MD) group (0.5  $\mu\text{g/kg/min}$ ), and suitable controls were used. The patients did not receive any premedication. In the operating room (OR), standard monitoring was performed using IntelliVue M8010A (Philips Electronics Japan, Tokyo, Japan) during the general anesthesia. Propofol (1.5 mg/kg) was administered for anesthetic induction 2 min after starting continuous infusion of remifentanil at a dose of 0.25  $\mu\text{g/kg/min}$  in the LD group and 0.5  $\mu\text{g/kg/min}$  in the MD group. Rocuronium (0.9 mg/kg) was also administered, and tracheal intubation was performed 3 min after anesthetic induction. Hemodynamic parameters [systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR)] and bispectral index (BIS) values were measured during anesthetic induction. Pulse oximetry oxygen saturation (SpO<sub>2</sub>), BP, HR, and BIS values were measured using pulse oximeter, cuff sphygmomanometer, EKG monitor, and BIS monitor ® (Aspect, BIS Monitor A-2000; Nihon Kohden, Tokyo, Japan), respectively. The values measured during a stable state immediately before the administration of remifentanil were recorded as the values for the pre-induction period. The lowest hemodynamic parameter values after induction and the highest hemodynamic parameter values during the 5-min period after intubation were recorded as the post-induction and post-intubation values, respectively. ESC of remifentanil was calculated using TIVA trainer™ (available at: <http://www.eurosiva.org/>; accessed on March 1, 2010), and intergroup comparisons were performed.

Differences in the gender and the American Society of Anesthesiologists-physical status (ASA-PS) scores were analyzed using the Mann–Whitney U test. The other demographic parameters and the ESCs of remifentanil were analyzed using an unpaired t test. The hemodynamic values were analyzed using a repeated-measures analysis of variance (ANOVA), and the intra- and intergroup multiple comparisons were performed using the Turkey–Kramer test and unpaired t test, respectively. Data were expressed as mean  $\pm$  SD, and a P value less than 0.05 was considered statistically significant.

## RESULTS

The patients' demographic characteristics showed no intergroup differences (Table 1).

**Table 1**

Patient Demographics

|                            | Low-dose group | High-dose group | P value |
|----------------------------|----------------|-----------------|---------|
| Number of patients         | 10             | 10              |         |
| Age (y)                    | 45 $\pm$ 14    | 41 $\pm$ 15     | 0.611   |
| Gender (M/F)               | 4/6            | 5/5             | 0.661   |
| Weight (kg)                | 55 $\pm$ 8     | 58 $\pm$ 9      | 0.391   |
| Height (cm)                | 163 $\pm$ 10   | 165 $\pm$ 11    | 0.559   |
| ASA physical status (I/II) | 8/2            | 7/3             | 0.615   |

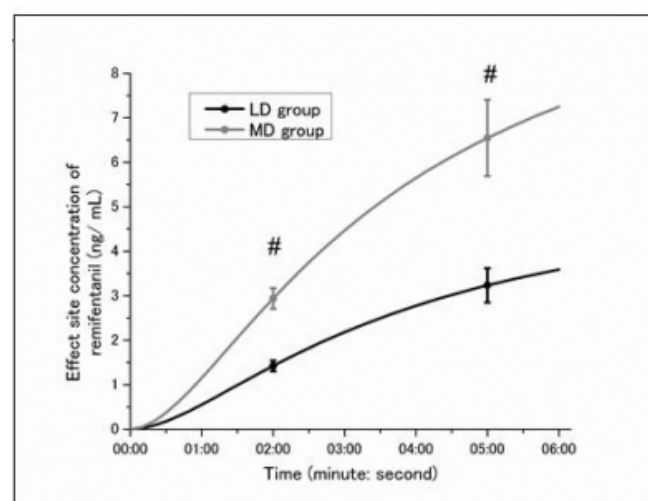
Data are presented as mean  $\pm$  SD or the number of patients. \*P < 0.05 was considered statistically significant.

ASA = American Society of Anesthesiologists

Throughout the anesthetic induction period, the SpO<sub>2</sub> levels were higher than 98% in all patients and no rigidity was observed. ESCs increased with time (Fig. 1).

**Figure 1**

Effect-site concentration of remifentanil  
Effect-site concentration (ESC) of remifentanil increases with time in both the groups. ESCs of remifentanil at anesthetic induction (2 min after starting administration) and tracheal intubation (5 min after starting administration) in the MD group (2.9  $\pm$  0.23 and 6.5  $\pm$  0.86 ng/mL, respectively) were significantly higher than the corresponding values in the LD group (1.4  $\pm$  0.11 and 3.2  $\pm$  0.38 ng/mL, respectively).



The remifentanil ESCs at induction and intubation in the MD group (2.9  $\pm$  0.23 and 6.5  $\pm$  0.86 ng/mL, respectively) were significantly higher than the corresponding values in

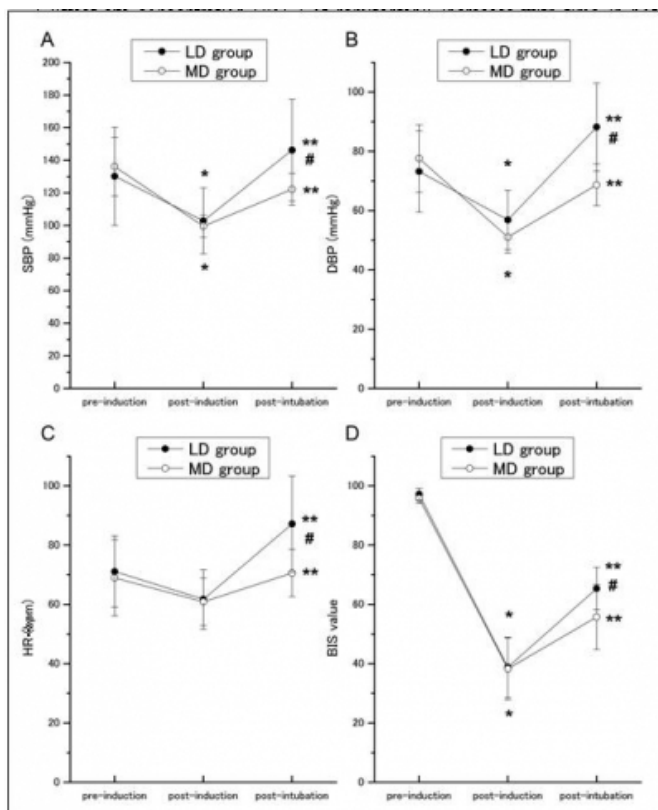
the LD group ( $1.4 \pm 0.11$  and  $3.2 \pm 0.38$  ng/mL, respectively). The hemodynamic values and BIS values at each period are presented in Fig. 2.

## Figure 2

The hemodynamic data and bispectral index (BIS) value for each period.

In both the groups (LD and MD), anesthetic induction caused a significant decrease in the systolic blood pressure (SBP; Fig. 1a), diastolic blood pressure (DBP; Fig. 1b), and BIS value (Fig. 1d). In both groups, tracheal intubation caused a significant increase in all the parameters, including the heart rate (HR; Fig. 1c). In the post-intubation period, all the parameters in group LD were significantly higher than those in group MD. However, in the pre-induction and pre-intubation periods, there were no significant intergroup differences in the parameter values.

\* $P < 0.05$ , when compared with the pre-induction values within the same group; \*\* $P < 0.05$ , when compared with the post-induction values within the same group; # $P < 0.05$ , when compared with the group standard at the same period. LD, low dose; MD, middle dose LD, low dose; MD, middle dose



In both the groups, anesthetic induction caused a significant decrease in the SBP, DBP and BIS values. In contrast, intubation caused a significant increase in all the parameters in both the groups. Because the degree of increase in each value in the LD group was higher than that in the MD group,

all the values in the LD group in the post-intubation period were significantly higher than the corresponding values in the MD group; in contrast, there were no significant intergroup differences between the values in the pre-induction and post-induction periods.

## DISCUSSION

Since rocuronium enables time interval between induction and intubation, it is necessary that the ESC of remifentanil was efficiently increased until intubation [1]. Antecedent administration is one of the methods used for increasing the ESC at intubation; however, (1) an excessive dose can cause respiratory problems such as desaturation during spontaneous breathing or result in a cannot-ventilate situation due to the rigidity during assisted ventilation and (2) an insufficient dose cannot suppress the stimuli caused by intubation [2]. In the present study, although the ESC of remifentanil in the MD group at anesthetic induction exceeded 2 ng/mL, which is not known to have a significant effect on the respiratory system [3], and reached 2.9 ng/mL, no respiratory complications occurred. It was thought that the above degree in the temporal increase in the concentration of remifentanil did not cause any symptom in consistent with that of a previous report in which anesthetic induction was safely performed with remifentanil doses ranging from 1 to 4 ng/mL [4]. Because the ESC of remifentanil in the MD group at intubation exceeded 6.0 ng/mL, which is known to be sufficient to blunt the cardiovascular response to intubation [5], and reached 6.5 ng/mL, the post-intubation hemodynamic and BIS values in the MD group were significantly lower than those in the LD group. Incomplete suppression may be attributed to the use of a propofol dose that was lower than that used in a previous report [4-5]. Although the ESC of remifentanil in the LD group at induction was 1.4 ng/mL, which is considered safe for the respiratory system, the ESC of remifentanil at intubation was only 3.2 ng/mL, which was considered insufficient for intubation according to a previous study [5].

The dose of anesthetics used in the present study may not be the optimal dose because innumerable combinations of propofol and remifentanil doses are possible [6-9]. The propofol dose used in this study (1.5 mg/kg) was based on that used in a previous report, in which  $1.4 \pm 0.1$  mg/kg propofol with a remifentanil ESC of 2 ng/mL was required for loss of consciousness [3]. However, other doses of propofol and remifentanil can also be selected for anesthetic induction. In addition, various doses of remifentanil may be

administered as the initial dose before continuous infusion or not administered at all. Moreover, the timing of administration of anesthetics can be changed.

This study is limited by the restricted population of patients (ASA, I or II and age, 20–64 years), small sample size, and the fact that only 2 drug combinations were evaluated.

Further studies must be conducted by including advanced patients or patients with obesity or severe complications.

Moreover, prophylactic use of or treatment with cardiovascular drugs should be taken into consideration when evaluating the optimal dose for anesthetic induction.

We found that administration of remifentanil at a dose of 0.5  $\mu\text{g/kg/min}$  during anesthetic induction with antecedent administration blunts the cardiovascular response to intubation and the increase in the BIS values due to intubation without causing any respiratory disorders or worsening suppressing of hemodynamics due to anesthetic induction. Therefore, we suggest that the 0.5  $\mu\text{g/kg/min}$  dose of remifentanil may be better than the 0.25  $\mu\text{g/kg/min}$  dose in this method of short-term anesthetic induction.

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