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Original Research Article

Effects of different remifentanil doses on the stress reaction and BIS value of video laryngoscope-guided tracheal intubation

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Abstract

Purpose: *To explore the affinity of different remifentanil doses for intravenous anesthesia in video laryngoscope-guided tracheal intubation.*
Methods: *Eighty patients who required anesthesia for elective non-ophthalmic surgery were included. They were divided into four groups (A, B, C and D) and received a different dose of either 1, 1.5, or 2 μg/kg remifentanil or a dose of 2 μg/kg fentanyl, respectively. An anesthetic state was achieved and maintained by administration of 3 - 5 mg/kg propofolum and 0.1 - 0.3 mg/kg remifentanil. The mean value of the various indices, including arterial pressure (MAP), bispectral index and heart rate (HR) were recorded prior to anesthesia induction (T0), prior to intubation (T1), instantly before intubation (T2), and at 1 (T3), 3 (T4) and 5 (T5) after the intubation. Cortisol concentration was measured at T0, T1 and T5.*
Results: *Remifentanil (1 μg/kg) induced a moderate increase in HR and MAP at T3 compared with fentanyl. HR and MAP in the lower dose group were significantly higher than those in groups B and C at T3. Compared to T1, the concentrations of cortisol decreased after anesthesia and then significantly increased during tracheal intubation. Cortisol concentration in group B was the lowest at T5.*
Conclusion: *The most effective concentrations of remifentanil are 1 and 1.5 μg/kg for anesthesia induction and tracheal intubation, respectively.*

Keywords: *Remifentanil, Stress reaction, Bispectral index, Video laryngoscope, Tracheal intubation*

INTRODUCTION

Tracheal intubation is a common practice for airway management. Historically, direct laryngoscopy (DL) has been the main option for performing oral laryngoscopy. However, tracheal intubation using direct laryngoscopy has a high incidence of complications, such as hypoxemia and hemodynamic instability, particularly in the Intensive Care Unit (ICU) [1-3]. Currently, there are new devices used to facilitate laryngoscopy and endotracheal intubation, one of which is the video laryngoscope (VL). It was developed to overcome the anatomic challenges associated with laryngoscopy; VL is mainly used in the operating room, the emergency room or in prehospital settings [4-7]. Noppens *et al* [8] found that when compared to DL, video laryngoscopy could improve the success rate of intubation and visual hierarchy in patients with difficult airway predictors. Despite these advantages, complications and stress reactions during administration still occur.

Many studies have shown that appropriate anesthetics can inhibit the stress reaction of tracheal intubation [9,10]. Remifentanil is a new opioid with fast onset (1-2 minutes) and short duration, making it ideal for reducing transient but noxious stimuli [11]. Due to its unique pharmacologic effects, remifentanil is widely used as clinical anesthesia. Previous reports on the use of remifentanil for tracheal intubation mainly focused on the type and dose selection of the anesthetic or the application of different intubation tools [12,13]. However, studies describing the prior administration of remifentanil with video laryngoscopy for tracheal intubation are rare.

In this study, VL following different doses of remifentanil was used for tracheal intubation. The perioperative stress reactions, Bispectral Index (BIS) and cortisol levels were detected and analyzed. The recommended respective doses of remifentanil were explored in this study. The purpose of this study was to explore the optimal dose of remifentanil for intravenous anesthesia in VL tracheal intubation.

EXPERIMENTAL

Patients

Eighty patients with American Society of Anesthesiology (ASA) physical status I-II and Mallampati class I-III admitted for elective abdominal surgery were included. There were 41 males and 39 females, aged 25 to 55 years. The height ranged from 160 to 175 cm, while the weight was between 54 and 73 kg. These patients had no cardiac, renal or central nervous system complications. The patients were randomized into four groups: 1 μg/kg remifentanil (group A), 1.5 μg/kg remifentanil (group B), 2 μg/kg remifentanil (group C) and 2 μg/kg fentanyl (group D). The study was approved by the Ethics Committee of Shouguang People Hospital, and all patients signed the intelligence agreement. The study also followed the guidelines of the Council for International Organizations of Medical Sciences (CIOMS International Ethical Guidelines) [14].

Anesthesia induction

The patients were admitted to the operating room and monitored for electrocardiogram, blood pressure, oxygen saturation and BIS. All of the patients were intravenous injected 0.04 mg/kg midazolam, 0.3 mg/kg etomidate, and 0.1 mg/kg vecuronium in sequence. Oxygen was supplied at 3 L/min using a mask, and an airway pressure between 15 and 20 cm H_2O was provided by manually assisted ventilation. Following loss of consciousness, the patients were given remifentanil or fentanyl. VL and tracheal intubation was processed for 60 s after the drugs in question were given by the same anesthesiologist who has more than 3 years of experience. If the first attempt at laryngoscopy and intubation was unsuccessful, the patients were excluded from the study.

Subsequently, mechanical ventilation was instituted with the ventilator at the following settings to achieve normocarbia (end tidal CO_2 35 – 40 mmHg): respiratory rate of 10-12 time/min and tidal volume of 8-10 ml/kg. No stimulus was given during mechanical ventilation. When the systolic blood pressure (SBP) decreased to < 90 mmHg for more than 60 s, 5-10 mg ephedrine or 2 mg dopamine was used. When the heart rate (HR) dropped to less than 55 bpm for over 1 min, 0.25 mg of atropine was administered.

Anesthesia maintenance

Propofol (3-5 mg/kg) and remifentanil (0.1 - 0.3 mg/kg) were intravenous infused for anesthesia.

Hemodynamic monitoring

The mean value of arterial pressure (MAP) and HR indexes were monitored prior to the induction of anesthesia (T0), prior to intubation (T1), instantly before intubation (T2), 1 min after intubation (T3), 3 min after intubation (T4) and 5 min after intubation (T5). Hypotension (a reduction in blood pressure < 30 % of baseline blood pressure) during induction was monitored and appropriately managed.

Depth of anesthesia monitoring

BIS values, indicating the depth of anesthesia, were recorded at T0, T1, T2, T3, T4 and T5.

Radioimmunoassay

At T0, T1 and T5, 3 ml of venous blood was taken from the patients of each group and centrifuged at 3500 r/min for 3 min. The obtained serum samples were then placed into polystyrene tubes and conserved in a -80°C refrigerator in order to determine the concentration of cortisol using radioimmunoassay.

Statistical analysis

Statistical analysis was processed by SPSS 16.0 software (SPSS, Chicago, IL, USA). The data were presented as mean ± standard deviation (SD). One-way ANOVA was applied for both intra-group and inter-group comparison. Chi-square test was used for comparing numerical data. *P* < 0.05 was set as the threshold of significance.

RESULTS

Clinical characteristics

A total of 80 patients participated in this study. Clinical characteristics, including age, sex and weight, are shown in Table 1. No significant difference occurred among the groups (*p* > 0.05).

Hemodynamics

No significant differences in the baseline HR and MAP were seen among the groups prior to anesthesia (Table 2). The parameters of HR and MAP decreased at T0 and increased from T2. As for the intragroup comparison, the HR and MAP values significantly decreased after anesthesia (P < 0.05 compared to T0). Furthermore, the MAP values at T3, T4, and T5 in group A and at T4 and T5 in groups B and C were much lower than those at T1 (P < 0.05). As for the intergroup comparison, the HR and MAP values were lower at T3 in groups B, C and D compared to that in group A (P < 0.05), except for an increase in HR for group C. Hypotension did not occur during anesthesia and intubation.

Depth of anesthesia

In each group, the BIS value notably decreased at T1, T2, T3, T4 and T5 (P < 0.05), compared with T0, below 65 between T1 and T5. The differences in values were not significant among the groups (P > 0.05) (Table 3).

Radioimmunoassay data

The concentrations of cortisol decreased in all 4 groups at T1 (*P* < 0.05 compared to T0) and then significantly increased at T5 in groups A, C and D (*P* < 0.05) compared to T1). Cortisol concentration in group B was the lowest among the four groups at T5 (*P* < 0.05) (Table 4).

Table 1: Clinical characteristics of patients (mean ± SD)

Characteristic	A	B	C	D
Sex (male/female)	13/7	16/4	15/5	12/8
Age (years)	43.5±11.3	44.5±9.1	45.2±15.3	46.8 ± 11.4
Weight (kg)	67.3 ± 9.8	66.8 ± 9.8	64.3±8.7	65.4 ± 9.1

Table 2: Hemodynamics indexes at different time points (n = 20, mean ± SD)

Index	Group	T0	T1	T2	T3	T4	T5
HR (times/min)	A	81.6 ± 9.0	74.6 ± 8.0▲	69.2 ± 9.7▲	76.3 ± 9.0▲▼	75.0 ± 9.0▲	73.9 ± 6.6▲
	B	78.7 ± 10.8	70.4 ± 9.2▲	64.5 ± 6.3▲	71.2 ± 6.8▲▼	72.6 ± 7.5▲	71.8 ± 6.3▲
	C	84.6 ± 13.0	79.3 ± 10.3▲	74.2 ± 8.4▲	75.6 ± 11.4▲	78.2 ± 9.6▲	79.4 ± 10.0▲
	D	82.8 ± 8.3	78.3 ± 8.8▲	70.6 ± 8.2▲	70.9 ± 7.2▲▼	72.3 ± 5.7▲	74.2 ± 5.5▲
MAP (mmHg)	A	96.4 ± 13.1	85.3 ± 8.6▲	74.0 ± 4.6▲	79.6 ± 3.0▲▼■	80.3 ± 3.9▲■	80.5 ± 5.5▲■
	B	95.6 ± 11.7	82.3 ± 8.4▲	71.4 ± 4.5▲	75.6 ± 3.1▲▼	78.5 ± 5.4▲■	78.4 ± 4.2▲■
	C	100.4 ± 9.2	84.9 ± 9.8▲	72.1 ± 7.1▲	73.7 ± 10.2▲▼	79.6 ± 9.0▲■	81.5 ± 7.2▲■
	D	92.4 ± 8.1	82.4 ± 8.3▲	74.0 ± 3.2▲	75.5 ± 4.4▲▼	77.1 ± 3.9▲	79.6 ± 3.1▲

MAP, mean arterial pressure; HR, heart rate; Intragroup comparison: with T0, ▲*P* < 0.05; with T1, ■*p* < 0.05; comparison among groups: with group A; ◆*p* < 0.05; with group D ▼*p* < 0.05

Table 3: BIS at different time points (n = 20, mean ± SD)

Group	T0	T1	T2	T3	T4	T5
A	90.4 ± 0.2	42.6 ± 3.0▲	60.4 ± 3.0▲	63.4 ± 2.9▲	56.6 ± 3.6▲	61.4 ± 2.6▲
B	93.2 ± 0.3	39.8 ± 4.7▲	62.8 ± 1.1▲	58.4 ± 2.6▲	56.7 ± 2.1▲	60.5 ± 3.1▲
C	94.3 ± 0.9	40.3 ± 2.6▲	60.0 ± 4.4▲	58.6 ± 3.3▲	57.4 ± 1.3▲	60.2 ± 3.5▲
D	92.4 ± 0.4	39.1 ± 4.8▲	61.9 ± 1.2▲	57.5 ± 2.7▲	55.8 ± 2.1▲	59.7 ± 3.0▲

BIS, Bispectral index; Intragroup comparison with T0, ▲*p* < 0.05

Table 4: Cortisol levels in the four groups at T0, T1 and T5 (n = 20, mean ± SD)

Group	T0	T1	T5
A	288.25 ± 13.35	262.61 ± 14.82▲	276.16 ± 10.68■
B	287.53 ± 13.79	261.45 ± 10.41▲	261.24 ± 12.87◆▼★
C	285.42 ± 10.01	259.35 ± 9.78▲	274.55 ± 9.84■
D	286.08 ± 12.78	261.49 ± 10.35▲	274.55 ± 15.68■

Intra-group comparison: Comparison with T0, ▲$p < 0.05$; comparison with T1, ■$p < 0.05$; Comparison among groups: comparison with A, ◆$p < 0.05$; with group D ▼$p < 0.05$; with group B ★$p < 0.05$

DISCUSSION

Generally, endotracheal intubation in the ICU is quite challenging due to the anatomic diversity and decompensated cardiopulmonary physiology of the patients. A series of significant complications including hypoxemia, aspiration, esophageal intubation, hypotension, dysrhythmias and cardiac arrest may occur in patients during tracheal intubation in the ICU [15]. The combined use of remifentanil and video laryngoscopy may reduce stress reaction during tracheal intubation. The purpose of this study was to explore the affinity of different remifentanil doses for intravenous anesthesia in video laryngoscope-guided tracheal intubation. In this study, 1 and 1.5 μg/kg are the more effective doses of remifentanil for anesthesia induction and tracheal intubation, respectively.

Comparing the results of VL and DL in the Emergency Department and Operating Room, data have shown improved performance using VL [16-19]. In a study by Jarrod *et al* [15], VL improved overall success rates and glottic visualization compared to DL in an ICU when operated by non-anesthesiology intensivists. Remifentanil is an opioid agent with an analgesic rapid onset of action. It effectively attenuates the hemodynamic response to laryngoscopy and tracheal intubation [20,21].

The effects of different doses of remifentanil on hemodynamics were studied. Hare *et al* [20] used three doses of remifentanil during the induction of anesthesia to control the hemodynamic responses associated with the laryngoscopy and endotracheal intubation. They found that higher remifentanil doses were sufficient to suppress the hemodynamic response to tracheal intubation. Moreover, 1 μg/kg remifentanil appeared to be an effective dosage to produce smooth intubating conditions in children [22]. Therefore, 1, 1.5 and 2 μg/kg were considered for remifentanil. In this study, a BIS < 65 was found in all four groups, but the differences in the values of BIS between the four groups were not significant (Table 3). BIS values between 40 and 65 suggested that patients were in an anesthetic state. When compared with fentanyl, remifentanil is typically used less in surgeries requiring anesthesia, although the application of remifentanil is significantly more effective for breathing and consciousness recovery [23]. It was found that a low dose of remifentanil (1 μg/kg, group A) induced a moderate increase in HR and MAP as a reaction to tracheal intubation at T3 compared to fentanyl (group D) (Table 2). Furthermore, HR and MAP values from low dose groups were higher than those in higher dose groups at T3. Interestingly, the effect of remifentanil on hemodynamics was less than fentanyl in tracheal intubation. This is possibly due to the higher affinity of remifentanil for the 5-HT 6 receptor [11].

Stress response is induced by a series of neuroendocrine reactions, especially sympathetic excitation [24] and excessive secretion of cortisol, that have a negative physiological effect. Cortisol concentration is important for stress reaction and stimulation, both of which may induce an increased release of cortisol [25]. In the current study, the concentrations of cortisol in all groups greatly decreased after anesthesia ($p < 0.05$). Cortisol concentration in group B was lowest among the four groups at T5 ($p < 0.05$), indicating that 1.5 μg/kg remifentanil is more efficient in inhibiting the stress response from laryngoscopy during tracheal intubation (Table 4). The reason for this is that remifentanil inhibits the secretion of norepinephrine and glucocorticoid [26]. These findings suggest that remifentanil has an inhibitory effect on these stress responses, although BIS < 60 does not completely inhibit the patient's stress response [27] .

There are several limitations in this study. The sample size was small, which might affect the feasibility of our results. The effects of remifentanil on stress reaction and BIS values of VL tracheal intubation were not compared to DL following tracheal intubation. Further, we observed only HR and MAP after VL tracheal intubation, which may not be sufficient for an absolute conclusion to this investigation.

CONCLUSION

The combined use of varying doses of remifentanil and VL markedly reduces the stress reaction caused by tracheal intubation. A dose of 1 μg/kg remifentanil for anesthesia induction and 1.5 μg/kg remifentanil for tracheal intubation is the most suitable strategy.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

YiboYuan and Lin Liu: conception and design and analysis of data. Shuqin Feng and Youtian Ma: drafting the article. Qingben Wang: revising the article critically for important intellectual content.

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