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ORIGINAL ARTICLE

The Optimal Effect-Site Concentration of Propofol for Endotracheal Suctioning in Intensive Care Unit Patients

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Objective: To evaluate the optimal effect-site concentration (Ce) of propofol during endotracheal suction (ETS) in the postoperative Intensive Care Unit (ICU) sedated patients. **Design and Setting:** The study design was a prospective randomized clinical study in a 13-bed ICU in a medical center. **Patients:** Thirteen mechanically ventilated patients were included in this study. **Methods:** All included postoperative patients received sedation by target-controlled infusion (TCI) of propofol under bispectral index (BIS) monitoring and 2–4 μg/kg/h fentanyl infusion for analgesia to keep numerical rating scale ≤4. While ETS was need, the sedation interventions were performed. We used the up-and-down method with a step size of propofol Ce 0.2 μg/ml for the next intervention. The sedation interventions of 1, 2, and 3 were baseline propofol Ce, baseline propofol Ce +0.2 mg/ml, and baseline propofol Ce +0.4 μg/ml, respectively. The predetermined propofol Ce was maintained for 5 min before ETS. Arterial systolic blood pressures (SBPs), arterial diastolic blood pressure (DBP), heart rates (HRs), and BIS before and after ETS were recorded. No moderate or severe coughing with limb movement was the primary outcome, and the surge of SBP, DBP, and HR ≤20% of baseline was the secondary outcome. **Results:** There were 39, 72, and 45 ETS were performed in the intervention 1, 2, and 3, respectively. In the primary outcome, the successful rates of ETS were 100%, 37.5%, and 15.4% in the intervention 3, 2, and 1, respectively ($P < 0.001$). In the secondary outcomes, the successful rates were 100% in all interventions. However, the surge of SBP ($P = 0.009$), DBP ($P = 0.025$), and HR ($P = 0.009$) were significant higher in the intervention 1 and 2 than the intervention 3. Right after the ETS, significant increase in BIS level was observed in the intervention 1 (13.9± 7.9) and 2 (14.4± 7.5) except for intervention 3 (−2.8± 14.5) ($P = 0.003$). **Conclusions:** An increase of propofol Ce 0.4 mg/ml for 5 min before ETS provided adequate sedation result in markedly attenuated ETS-induced coughing, limb movement, and hyperdynamic status during ETS while the use of TCI propofol sedation in postoperative ICU patients.

Key words: Propofol, target-controlled infusion, endotracheal suctioning, bispectral index, Intensive Care Unit

INTRODUCTION

Ensuring adequate sedation is important to critical patients; however, maintenance of "adequate" sedation remains difficult.[1] Because physical stimuli are frequently encountered in the routine care of Intensive Care Units (ICUs) patients, such as nursing, endotracheal suction (ETS), physiotherapy, and any mobilization.[2]

Of the various sedation scales reported, the Ramsay sedation score (RSS) is the most widely used.[3] However, objective tools to assess the impact of these stimuli on awareness or analgesia of critically ill patients are scarce. Bispectral index (BIS) has recently been developed to monitor depth of anesthesia, and the level of BIS was correlated with the level of hypnosis.[4] Previous investigations have showed that BIS monitor in ICU may help improve sedation and even during invasive events.[5-7]

ICU patients sedated with propofol had a reduced risk of mortality and had both an increased likelihood of earlier ICU discharge and earlier discontinuation of mechanical

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ventilation.[8] Propofol infusion with syringe pump given at a rate of 0.71 ± 0.31 mg/kg/h would be sufficient to produce a sedation with RSS value between 2 and 3 in ICU.[9] In addition, target settings in the range of 0.2–2.0 μg/ml of propofol by target-controlled infusion (TCI) provided adequate sedation in adult ICU.[10]

Patients in ICU needed ETS for respiratory care to remove excess respiratory secretions and to improve respiratory function. Until now, the research on bolus dosage of propofol or the optimal effect-site concentration (Ce) of propofol during routine nursing care such as ETS and physiotherapy without triggering severe coughing or limb movement or unstable hemodynamic status is unclear. The aim of this study is to assess the optimal Ce of propofol by TCI and BIS variations for ETS in ICU sedated patients.

METHODS

This study was approved by the Ethics Committee (TSGHIRB No: 099-05-191) of Tri-Service General Hospital, Taipei, Taiwan (Chairman, Professor Pauling Chu), on 22nd of December, 2010. All patients' family provided written informed consent before being enrolled in this study.

Thirteen patients hospitalized in a 13-bed ICU in a medical center were included (January 2011–December 2011) in this study. The inclusion criterion was patients received major open abdominal surgeries and need mechanical ventilation support at least 1 day with intravenous sedation and analgesia postoperatively. Exclusion criteria were: (1) renal failure (creatinine clearance <50 ml/min), (2) liver failure (prothrombin time <30% or hepatic encephalopathy), (3) intracranial evolving disease (brain injury, brain tumor, abscess, stroke, or hemorrhage), (4) patients paralyzed for any reason, (5) body mass index >30, (6) American Statistical Association ≥4, (7) septic shock or severe sepsis, and (8) use of inotropes. All postoperative patients received intravenous fentanyl 2–4 μg/kg/h for analgesia to keep numerical rating scale ≤4, and continuous infusion of propofol (fresfol 1%) using the Schneider kinetic model of TCI system (Fresenius Orchestra Primea®, France) with Ce adjusted according to BIS 65–85 in the daytime and 60–70 in the nighttime.[4,11]

The intervention 1, 2, and 3 were baseline Ce, baseline Ce +0.2 μg/ml, or baseline Ce +0.4 μg/ml, respectively. Initially, every patient received ETS at intervention 1 and then we used up-and-down method with Ce of propofol 0.2 ug/ml. The predetermined Ce of propofol was maintained for 5 min before ETS. The interventions were completed while the patients were extubated. ETS was performed by the nurse, and the interventions were performed when clinically indicated to maintain the patency of the endotracheal tube. Before doing ETS, preoxygenation with 100% O_2 was given. The duration of each ETS was <15 s. Moreover, the negative pressure of ETS was <150 mmHg.[12] Patients' demographic characteristics were recorded. Thirty seconds before and after ETS, arterial systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), BIS, and RSS were recorded. The recorder was blinded to the interventions. The primary outcome was defined as no moderate to severe coughing with limb movement,[13] and the secondary outcome was defined as the hemodynamic changes ≤20% of baseline. Results are expressed as mean with standard deviation for BIS level, RSS, HR (bpm), and SBP and DBP (mmHg). We used hierarchical generalized linear model to show differences of BIS level, RSS, HR, and SBP and DBP between pre- and post-ETS. A P <0.05 was considered significant. The statistics was performed using SPSS version 18.0 for Windows.

RESULTS

Thirteen postoperative patients were included in this study with a total of 156 ETS. There were 39, 72, and 45 ETS were performed in the intervention 1, 2, and 3, respectively. The patients' characteristics and surgical procedures were shown in Table 1. The descriptive information was shown in Tables 2 and 3. The patients comprised 12 men and 1 woman, with age 49.1 ± 19.8 years, weight 73.0 ± 16.1 kg, and height 168.2 ± 8.0 cm. Pre-ETS Ce was 0.9 ± 0.4, and post-ETS Ce was 1.1 ± 0.4 mg/ml [Table 1]. In the primary outcome, the successful rates of ETS were 100%, 37.5%, and 15.4%

Table 1: Patient's characteristics

Age (year)	49.1±19.8
Gender (male/female)	12/1
Height (cm)	168.2±8.0
Weight (kg)	73.0±16.1
Pre-ETS Ce (μg/ml)	0.9±0.4
Post-ETS Ce (μg/ml)	1.1±0.4
Systemic disease (*n*)	
Hypertension	3
Diabetes	2
Surgical procedure (*n*)	
Gastrectomy	9
Biliary tract surgery	3
Exploratory laparotomy with splenectomy	1

Values are expressed as mean±SD except for gender.
Pre-ETS=Preendotracheal suction; Post-ETS=Postendotracheal suction; Ce=Effect-site concentration of propofol; SD=Standard deviation

in the intervention 3, 2, and 1, respectively ($P < 0.001$). Before the interventions, BIS levels were 72.9 ± 6.3, 69.8 ± 9.1, and 64.4 ± 14.2, in the intervention 1, 2, and 3, respectively ($P = 0.021$). Right after ETS, significant increase in BIS level was observed in the intervention 1 (13.9 ± 7.9) and 2 (14.4 ± 7.5) except for intervention 3 (−2.8 ± 14.5) ($P = 0.003$). In the secondary outcome, the successful rates were 100% in all interventions. However, significant SBP (mmHg) surge (intervention 1 - 19.0 ± 13.0, intervention 2 - 12.6 ± 9.9, and intervention 3 - 3.7 ± 8.9, $P = 0.009$), DBP surge (7.4 ± 7.8, 8.1 ± 5.6, and 0.8 ± 5.8 in intervention 1, 2, and 3, respectively, $P = 0.025$), and HR surge (intervention 1 - 7.8 ± 8.5, intervention 2 - 4.5 ± 5.4, and intervention 3 - −0.8 ± 3.4, $P = 0.009$) were observed [Tables 2 and 3]. Dose-response table was shown as Table 4.

No patient underwent treatment with epinephrine or norepinephrine or antihypertensive drug during the study. No variation in oxygen saturation was observed in the studied patients. Besides, there was no atelectasis or wound infection in the studied cases.

Table 2: Comparison of the secondary outcome for the three groups

	Intervention 1 (*n*=39)		Intervention 2 (*n*=72)		Intervention 3 (*n*=45)	
	Mean±SD	*P*	Mean±SD	*P*	Mean±SD	*P*
Pre-ETS RSS	2.83±0.74	0.04	2.63±0.58	0.017	2.67±0.50	0.865
Post-ETS RSS	2.57±0.94		2.32±0.53		2.68±0.62	
Pre-ETS BIS	72.9±6.3	<0.001	69.8±9.1	<0.001	64.4±14.2	0.629
Post-ETS BIS	86.8±7.9		84.2±7.5		61.6±6.9	
Pre-ETS SBP	123.1±21.0	<0.001	127.8±24.4	0.001	134.9±20.3	0.221
Post-ETS SBP	142.1±27.6		140.4±23.7		138.6±24.7	
Pre-ETS DBP	61.4±12.5	0.007	65.2±12.6	<0.001	70.3±7.9	0.682
Post-ETS DBP	68.8±15.0		73.2±12.0		71.1±10.4	
Pre-ETS HR	99.6±21.6	0.009	99.7±16.9	0.011	98.6±12.5	0.495
Post-ETS HR	107.3±22.9		104.6±16.5		97.8±11.2	

Data shown as mean±SD. RSS=Ramsay sedation score; Pre-ETS=Preendotracheal suction; Post-ETS=Postendotracheal suction; SD=Standard deviation; HR=Heart rate

DISCUSSION

This study is the first to investigate the optimal propofol Ce using TCI system for daily nursing routine care, ETSs in the postoperative critically ill patients. We found that the optimal Ce of propofol for blunting coughing reflex, limb movement, and keeping hemodynamics stable during ETS appears to be 0.4 μg/ml above the baseline Ce of propofol sedation by the TCI system.

Patients admitted to ICU require respiratory care and in particular ETS to remove excess respiratory secretions to improve respiratory function.[14] ETS is one of the most common supportive measures and procedures; it performed in every patients with artificial airways.[15] Despite being a necessary procedure, it can lead to complications, such as lesions in the tracheal mucosa, pain, discomfort, infection, alterations of the hemodynamic parameters and of the arterial gasses, bronchoconstriction, atelectasis, increase in intracranial pressure, and alterations in cerebral blood flow.[12,16] Gray *et al*.[17] showed ETS-induced excessive coughing, and it may cause hypoxia/hypoxemia. Previous studies reported ETS-induced hypertension and tachycardia,[18,19] and these may cause unstable hemodynamic status. In our study, the hemodynamic changes were acceptable; however, only 15.4% and 37.5% ETS were successful in intervention 1 and 2, without moderate or severe coughing; therefore, we suggested that an additional bolus of propofol was need before ETS to improve care quality and patient comfort. Moreover, in clinical, the optimal dosage of propofol without triggering coughing, limb movements, and unstable hemodynamic status during ETS is unclear.

Daily sedation interruption and targeting light sedation levels are safe and proven to improve outcomes for sedated ICU patients when these approaches result in reduced sedative exposure and facilitate arousal.[20] Total intravenous anesthesia with TCI system has been used in clinical anesthesia.[21-31] In an individual patient, titration of the target setting to achieve the depth of sedation desired is necessary, and the ease and precision of this titration is facilitated by the TCI system. Previous study demonstrated that effective sedation can be achieved with TCI

Table 3: Changes of the secondary outcome for the three groups

	Intervention 1 (*n*=39)	Intervention 2 (*n*=72)	Intervention 3 (*n*=45)	*P*
Post-ETS RSS - pre-ETS RSS	−0.26±0.39	−0.31±0.40	0.01±0.18	0.088
Post-ETS BIS - pre-ETS BIS	13.9±7.9	14.4±7.5	−2.8±14.5	0.003
Post-ETS SBP - pre-ETS SBP	19.0±13.0	12.6±9.9	3.7±8.9	0.009
Post-ETS DBP - pre-ETS DBP	7.4±7.8	8.1±5.6	0.8±5.8	0.025
Post-ETS HR - pre-ETS HR	7.8±8.5	4.5±5.4	−0.8±3.4	0.009

Data shown as mean±SD. Pre-ETS=Preendotracheal suction; Post-ETS=Postendotracheal suction; SD=Standard deviation; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; RSS=Ramsay sedation score; HR=Heart rate

Table 4: Dose-response table

Increased Ce from baseline (μg/ml)	Baseline	Baseline + 0.2	Baseline + 0.4
Case 1 (success/fail)	1/2	2/3	3/0
Case 2 (success/fail)	0/2	2/3	3/0
Case 3 (success/fail)	0/3	2/3	3/0
Case 4 (success/fail)	0/3	2/3	3/0
Case 5 (success/fail)	0/3	2/3	3/0
Case 6 (success/fail)	0/2	1/5	5/0
Case 7 (success/fail)	1/3	3/3	3/0
Case 8 (success/fail)	0/2	1/5	5/0
Case 9 (success/fail)	1/3	3/3	3/0
Case 10 (success/fail)	1/2	2/4	4/0
Case 11 (success/fail)	1/2	2/4	4/0
Case 12 (success/fail)	0/3	2/3	3/0
Case 13 (success/fail)	1/3	3/3	3/0
Total (success/fail)	6/33	27/45	45/0

Ce=Effect-site concentration of propofol

of propofol in adult ventilated patients, and the blood propofol concentration settings required to achieve an optimum depth of sedation were generally within the range of 0.2–2.0 μg/ml.[10] Therefore, we used continuous propofol infusion through TCI system and kept light sedation for the patients as previous study recommended.[20] Brocas *et al*. used additional alfentanil bolus before ETS due to rapid onset of alfentanil for analgesia.[7] However, we used an increase of propofol Ce before ETS due to the cheaper and easily available reason. In spite of the two different mechanisms, both results were acceptable for ETS.

Propofol, administered by conventional rate-controlled infusion, is an effective sedative in critically ill patients.[32-35] However, hypotension may be observed while oversedation, and hyperdynamic status with coughing and limb movement may be observed while insufficient sedation during daily routine nursing care. The use of TCI sedation technique is effective and safe and has a better acceptability than the manually controlled infusion technique.[36]

BIS-guided sedation monitoring resulted in a marked reduction in the total dose of sedative used to achieve the same level of clinical sedation resulting in shortened time to wake up.[11] In addition, McMurray *et al*. reported that using TCI of propofol combination with a modified RSS achieved a desired level of sedation in ICU patients.[10] In our study, we showed that the BIS level around 65; the sedation level was enough to cover the ETS stimulation. However, up to now, BIS-guided sedation monitoring to adjust TCI of propofol in ICU sedation is needed to further investigate.

There are some limitations to our study. First, few patients (n = 13) were enrolled, but the size of the sample enabled us to show a statistical difference for the primary end-point (coughing and limb movement). Second, we merely included the postoperative patients and one woman, so the population of medical ICU patients and female were needed to further investigate. Third, we used easily available sedation technique with increased Ce of propofol instead of adding analgesics for ETS because we had used continuous infusion of fentanyl. Thought both two methods (add sedatives and analgesics) were acceptable for ETS in ICU, further investigations were needed.

CONCLUSION

An ideal increase of propofol target concentration to decrease the likelihood of cough and limb movements and unstable hemodynamic status during ETS may be 0.4 μg/ml with intravenous fentanyl 2–4 μg/kg/h in postoperative patients.

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Conflicts of interest

There are no conflicts of interest.

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