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Optimal effect-site concentration of propofol for tracheal suctioning during emergence from ophthalmic surgery

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Abstract

In ophthalmic surgery, coughing during emergence from general anesthesia may have a detrimental effect on intraocular pressure. Tracheal suction during emergence may elicit this reflex. The optimal effect-site concentration (EC) of propofol to prevent triggering of the cough reflex during tracheal suctioning is unknown. The aim of this study is to assess the optimal EC of propofol for tracheal suctioning during emergence in patients undergoing ophthalmic surgery.

Twenty-one patients were enrolled, all of them American Society of Anesthesiologists (ASA) physical status I or II non-smokers undergoing ophthalmic surgery. Anesthesia was induced and maintained under total intravenous anesthesia using target-controlled infusion. During emergence from general anesthesia, tracheal suction was performed at different propofol concentrations as required for Dixon's up-and-down method with a step size of 0.2 μg/ml. A propofol concentration at which the cough reflex was not triggered during tracheal suctioning was considered successful.

The EC_{50} of propofol for tracheal suction without cough was 1.4 μg/ml and the EC_{95} was 1.6 μg/ml.

Tracheal suction may be accomplished without triggering the cough reflex when the propofol effect-site concentration is higher than 1.6 μg/ml.

Abbreviations: ASA = American Society of Anesthesiology, BIS = bispecrtal index, EC = effect-site concentration, $EtCO_2$ = end-tidal carbon dioxide, GA = general anesthesia, SD = standard deviation, TCI = target controlled infusion, TIVA = total intravenous anesthesia.

Keywords: cough, emergence from anesthesia, ophthalmic surgery, propofol, tracheal suction

1. Introduction

Cough is an important protective reflex to enforce the clearance of secretions and prevent aspiration. The reflex is frequently encountered during emergence from general anesthesia due to irritation of the tracheal tube or tracheal suctioning and can induce adverse effects.[1–4] During thoracic or abdominal surgery, an episode of severe coughing can induce high intrathoracic and intraabdominal pressure with consequent bleeding, and severe cough occasionally results in wound rupture. In ophthalmic surgery or neurosurgery, suppression of the cough reflex should be achieved to prevent elevated intraocular and intracranial pressures.[2,4] On the other hand, the reflex induced by tracheal suctioning during emergence and extubation may be essential in some patients who are heavy smokers or have pulmonary diseases because heavy accumulation of sputum may increase the risk of pulmonary complications.

Several medications and techniques have been found to prevent cough during emergence from anesthesia.[5–14] However, the relationship between the optimal effect-site concentration (EC) of propofol and the cough reflex induced by tracheal suctioning during the emergence from propofol/fentanyl anesthesia remains unknown. In this study, we assessed the optimal EC of propofol for tracheal suction during emergence from total intravenous anesthesia (TIVA) in ophthalmic surgery.

2. Methods

After obtaining approval of the Institutional Review Board of the National Defense Medical Center (TSGHIRB No: 100-05-005, Taipei, Taiwan) and written informed consent from patients, 21 adults scheduled for elective ophthalmic surgery under intubated TIVA using a target-controlled infusion (TCI) system (Fresenius Orchestra Primea, France) were enrolled in this study. The eligible patients were non-smokers aged 39 to 75 years with ASA

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physical status I or II. To eliminate performance bias, only patients whose surgical duration was under 2 hours were included.[8] Patients with history of recent upper respiratory infection, asthma, chronic respiratory disease, gastro-esophageal reflux disease, cardiovascular accidents, uremia, liver function impairment or ASA physical status ≥III were excluded. In such patients, impaired cough reflex or hypersensitivity of airway may interfere with the predicted concentration of propofol.[15,16]

No patient received premedication prior to the induction of anesthesia. Standard anesthetic monitors were used for all patients, included electrocardiography (lead II), pulse oximetry, non-invasive blood pressure, respiratory rate, and end-tidal carbon dioxide ($EtCO_2$) pressure. Furthermore, depth of anesthesia was monitored by bispectral index (BIS) throughout the procedure. TIVA was induced with i.v. fentanyl 2 μg/kg and 2% lidocaine 1.5 mg/kg. Continuous infusion of propofol (Fresofol 1%) was administered via the Schnider kinetic model TCI system with an EC of 4.0 μg/ml. When the patient lost consciousness, 0.6 mg/kg of rocuronium was given to facilitate tracheal intubation.[17,18] The tracheal tube size was 6.5 mm and 7.0 mm (internal diameter; ID) for women and men, respectively. The tracheal cuff was inflated with air to a pressure of 20 cm H_2O. Propofol was adjusted to keep the BIS values in a range from 40 to 60 during maintenance of anesthesia, with the EC for the propofol TCI was titrated up or down by 0.2 μg/ml if the BIS values exceeded the recommended range. Mechanical ventilation was maintained with volume controlled mode using a tidal volume 6 to 8 ml/kg (even at the time of tracheal suctioning) and was adjusted to maintain $EtCO_2$ pressure at 35 to 45 mm Hg. Neuromuscular blockade and analgesia were complemented with rocuronium (10 mg, i.v.) and fentanyl (50 mcg i.v.), respectively, as needed during surgery. At the end of surgery, the lungs were ventilated with 100% oxygen at a fresh gas flow of 6 l/min. Restoration of neuromuscular function was achieved by administering neostigmine (0.03–0.04 mg/kg) with glycopyrrolate (0.006–0.008 mg/kg) to antagonize neuromuscular blockade once spontaneous breathing had returned. The target propofol concentration for suctioning was adjusted by using Dixon's up–and down sequential method.[19] The initial propofol concentration of the first patient was 2.0 μg/ml. Tracheal suction was performed when the preset propofol concentration was reached. If no cough was observed during tracheal suctioning, the setting was considered successful; cough during tracheal suctioning was defined as failure. The step was not considered as a failure if cough occurred before or after tracheal suctioning. The next setting of propofol concentration was predetermined by the response of previous patient with a higher or lower dose (0.2 μg/ml as a step size). After a failure trial, the target concentration of propofol was increased by 0.2 μg/ml for next patient. Conversely, if no cough was observed, the propofol concentration was decreased by 0.2 μg/ml for next patient. The results of predetermined propofol concentrations during tracheal suctioning were recorded. In addition, the BIS value was 50 to 70 at the time of tracheal suctioning, because of the different propofol CE.

Demographic data were collected and are presented as mean and standard deviation (SD). Dixon's up-and-down method needs six pairs of failure-success for statistical analysis, and sample size came from the basis of Dixon's method. The up-and-down sequences were also analyzed by Probit analysis, which enabled us to derive the target propofol concentration for suctioning with 95% confidence limits of the mean. We also analyzed our data using a logistic regression test to obtain the probability of no cough versus EC, the maximum likelihood estimators of the model variables, and a goodness of fit.

Table 1

Patients' characteristics and the duration of anesthesia.

Age (yr)	60.8 (8.7)
Gender (M/F)	11/10
Height (cm)	163.1 (7.9)
Weight (kg)	65.4 (8.8)
Anesthetic time (mins)	82.7 (12.7)

Values are expressed as mean (SD) except for gender.

3. Results

Twenty-one patients were included in this study. The patients' demographic data and the duration of the anesthesia time are presented in Table 1. The plots of propofol EC associated with success or failure of tracheal suction for each consecutive patient are shown in Fig. 1. The EC_{50} for tracheal suction during emergence without cough in 50% of adults was 1.4 μg/ml (Fig. 2). The dose-response curve constructed by probit analysis on the patients' data revealed that EC at which 95% of patients had tracheal suction without cough (EC_{95}) was 1.6 μg/ml (Fig. 2).

4. Discussion

The major finding in our study is that tracheal suctioning rarely induced cough reflex at a propofol EC equal to 1.6 μg/ml, while the incidence of cough increased below this concentration. Accordingly, we suggest that tracheal suction can be performed without cough responses before the propofol EC drop to 1.6 μg/ml during TIVA with intermittent bolus of fentanyl in ophthalmic surgery.

Cough is a physiological response for cleaning the secretion or particulates from the airways to prevent pulmonary aspiration or infection. The cough reflex can be triggered by noxious stimuli, including tracheal tube placement, sputum retention, irritant halogenated anesthetics and tracheal suctioning during general anesthesia. Unfortunately, coughing during anesthesia can cause damage including detrimental hemodynamic fluctuations and increased intraocular and intracranial pressures.

During emergence from general anesthesia, tracheal irritation is the major cause of the cough reflex.[20] Therefore, suction of secretions from tracheal tube should be limited or cautious to prevent sudden coughing or bucking during maintenance and emergence from anesthesia, especially in ophthalmic surgery, otological surgery, and neurosurgery. In these circumstances, there are several medications and techniques to mitigate cough response during emergence from anesthesia. These methods included the use of laryngeal mask,[11] extubation at a deep level of anesthesia,[13] administration of short-acting opioids,[10,12] dexmedetomidine,[7] or intravenous local anesthetics, application of local anesthetics or steroids around the cuff,[5,8,9] non-irritant halogenated anesthetics.[6,14] Some studies have shown that TIVA is associated with less cough response, more stable hemodynamics status,[15,21,22] faster emergence and less postoperative nausea and vomiting than volatile anesthesia.[17,18] Although choosing TIVA as anesthetic technique may lead to inhibition of airway reflexes, a high possibility of eliciting the cough reflex remains in the presence of noxious stimuli (intubation and suctioning).

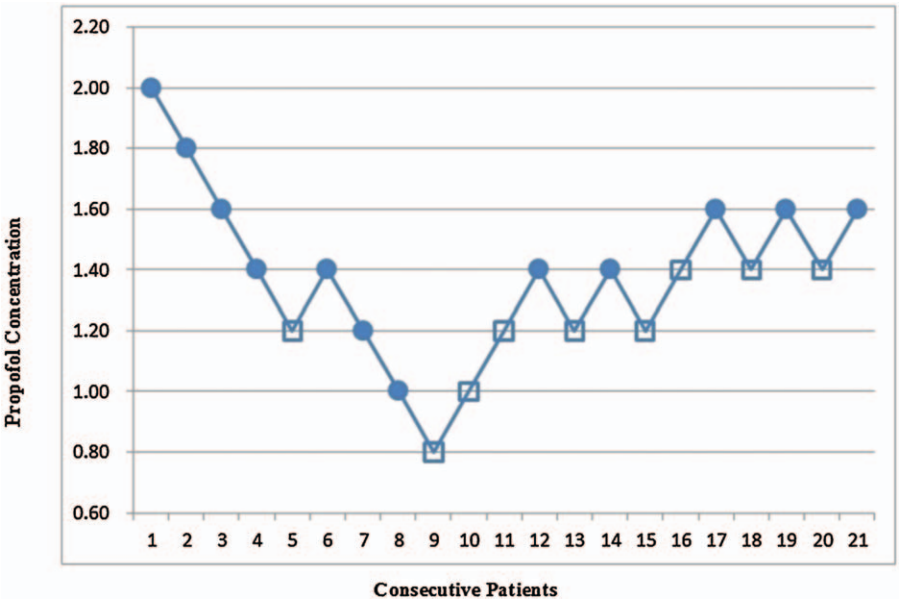

Figure 1. The propofol EC in the 21 consecutive patients in whom the tracheal suction was attempted. Each patient's data are represented with a circle or a square; a filled circle (●) means successful suction, a hollow square (□) means unsuccessful suction. The EC at which a successful suction was possible in 50% of patients was 1.4 μg/ml.

It seemed reasonable to avoid airway suction in attempt to diminish the stimulation. Nonetheless, this approach is not feasible in prolonged anesthesia or patients with pulmonary diseases such as chronic obstructive pulmonary disease or ongoing respiratory tract infection. Gentle tracheal suction is necessary to clear sputum and to minimize postoperative pulmonary complications in intubated patients. In addition, the use of TIVA technique (propofol/remifentanil) may increase more salivary excretion than sevoflurane anesthesia.[23] Accumulation of sputum and excessive production of saliva can increase tracheal stimulation during the maintenance and emergence from anesthesia. Moreover, retention of sputum may predispose patients to respiratory complications such as bronchial atelectasis, pulmonary aspiration, and pulmonary infection. Therefore, implementing suction without triggering cough reflex can be an important issue.

Deeper residual anesthetic depth will be responsible for lower incidence of cough during extubation.[15,24] There have been many reports on the effects of anesthetics on the cough reflex, especially regarding the effect of subhypnotic concentrations of anesthetics in the recovery period. Subhypnotic doses of sevoflurane or propofol may influence cough responses during emergence from anesthesia.[24] Several investigations have focused on the EC of remifentanil on the cough response during extubation.[24,25] Lee et al[24] found that the EC_{95} of remifentanil for cough suppression during extubation under propofol is 1.96

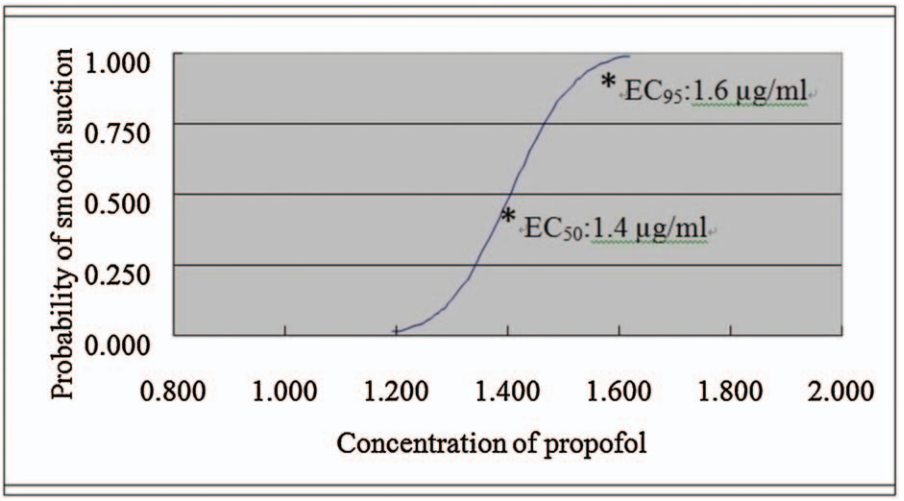

Figure 2. Dose-response curve for propofol from the probit analyses of individual concentrations and the respective patient reactions to tracheal suction. The concentrations at which there were 50% and 95% probabilities of successful suction were 1.4 μg/ml and 1.6 μg/ml, respectively.

ng/ml and under sevoflurane is 2.43 ng/ml. Jun et al[25] showed the predicted remifentanil concentration at 1.5 ng/ml during emergence from sevoflurane anesthesia suppressed coughing without serious adverse events in elective thyroidectomy. These studies focused on the EC of remifentanil needed to suppress cough response during extubation, rather than fentanyl or propofol. Kazama et al[26] found that the plasma propofol concentration at which 50% of patients do not develop gag or somatic responses to insertion of gastroscope in middle-aged (50–69 year) patients was 2.34 μg/ml. Lin et al[27] found that the optimal propofol concentration during flexible bronchoscopy ranged from 2.1 to 2.4 μg/ml after bolus of 5 μg/kg alfentanil. Guglielminotti et al[28] reported that the cough reflex induced by nebulized citric acid could not be suppressed by the estimated propofol concentrations less than 1.2 μg/ml after colonoscopy under propofol sedation without airway instrumentation. Therefore, we speculate that the stimulus intensities of tracheal suction were lower than those of insertion of gastroscope and flexible bronchoscope but higher than those of insertion of colonscope without airway instrumentation.

There are several limitations to our study. First, smoking may alter airway sensitivity and thereby influence the cough response during emergence from anesthesia. Some studies have shown that smokers are prone to coughing during volatile anesthesia while others showed no significant effect.[6,15,20] Because smokers were not included in our study, further studies will be needed to discover whether smoking affects our conclusion. Second, we used intermittent i.v. bolus fentanyl but not continuous infusion of remifentanil during the study. The association between propofol and narcotics with suppression of cough reflex remained unknown. Thus, it is difficult to discover the optimal EC of propofol for preventing coughing while using different narcotics. The third limitation is patient age. The elderly may be vulnerable to the decreased sensitivity of cough reflex[29] and the amnesic effect of propofol. In our study, patient age ranged from 39 to 75 years old (mean age 60.8). Further studies using different age groups may be desirable. The fourth limitation is geographical disparity in the allocation; the results are conceivably applicable only for the Chinese and not appropriate for other populations. Finally, the effect of residual effect of neuromuscular function on cough reflex during tracheal suctioning must be considered. We did not routinely use monitor neuromuscular blockade in minor surgeries such as breast cancer surgery or ophthalmic surgery in Taiwan. However, we administrated neostigmine with glycopyrrolate to antagonize neuromuscular blockade once spontaneous breathing had returned (the train-of-four ratio might be > 0.7[30,31]) at the time of tracheal suctioning.

In conclusion, the optimal propofol EC for tracheal suction should be higher than 1.6 μg/ml during TIVA with propofol and fentanyl in ophthalmic surgery.

Author contributions

Conceptualization: Shun-Ming Chan.
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Validation: Yi-Hsuan Huang.
Writing – original draft: Nan-Kai Hung.
Writing – review & editing: Meei-Shyuan Lee, Hou-Chuan Lai, Bo-Feng Lin, Shun-Ming Chan, Zhi-Fu Wu.

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