The Effect-site Concentration of Propofol Required for the Replacement of an Endotracheal Tube by a ProSeal Laryngeal Mask Airway in Neurosurgical Patients

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Introduction

Rapid emergence from anesthesia and prompt neurologic assessment allow early detection of intracranial complications after neurosurgical procedures. (1-4) Recovery from general anesthesia, however, is usually associated with sympathetic stimulation and catecholamine release, which cause tachycardia, hypertension and systemic vasoconstriction. (5-7) Moreover, coughing or bucking during tracheal extubation increases intracranial pressure by increasing intrathoracic pressure, cerebral venous pressure and cerebral blood volume. (5,8) These metabolic and hemodynamic changes can result in hazardous complications such as intracranial hemorrhage, cerebral edema or ischemia. (1,2,5) The methods suggested to attenuate these responses include a tracheal extubation with the patient deeply anesthetized or an administration of lignocaine or anti-hypotensive agents. (8) Some researches demonstrated that the adverse hemodynamic alterations could have been prevented by exchanging an endotracheal tube for a laryngeal mask airway (LMA). The LMA in place of an endotracheal tube provided a patent airway and alleviated the straining of patients during emergence. (9-12) If such an exchange is attempted under inadequate level of anesthesia, however, it may be accompanied by coughing, bucking, airway obstruction or stress responses and consequently, this method cannot offer any benefits.

We performed this study to determine the effect-site concentration of propofol required to substitute a ProSeal LMA (PLMA) for an endotracheal tube in patients undergoing elective neurosurgical procedures under total intravenous anesthesia (TIVA) with propofol and remifentanil.

Materials & Methods

After obtaining an approval of institutional ethics committee and written informed consents, we enrolled 26 adult patients, ASA physical status I or II, aged
21-70 years, who were scheduled for elective neurosurgical procedures under TIVA. The patient was excluded from our study if he or she had known or expected difficult airway; had a risk factor of gastric aspiration; had allergy or hypersensitivity to any of the drugs used; or required a position other than supine. The one who presented difficulty in mask ventilation or tracheal intubation was also ruled out.

No sedative or opioid premedication was given before surgery. When a patient arrived at an operating room, radial arterial catheterization was performed under local anesthesia. The patient was also monitored with an electrocardiogram, a pulse oximeter and a peripheral nerve stimulator applied to ulnar nerve at the wrist. Anesthesia was induced with propofol and remifentanil using a target controlled infusion system (Orchestra® Base Primea, Fresenius Vial, France), and endotracheal intubation was achieved following neuromuscular blockade with rocuronium 0.6 mg/kg. Mechanical ventilation with mixture of oxygen and air was controlled to maintain normocarbia. Anesthesia was maintained with a continuous infusion of propofol and remifentanil, and their target effect-site concentrations were adjusted based on the hemodynamic responses of the patients. Rocuronium was administered intermittently to maintain 0 or 1 response to train-of-four (TOF) stimulation until 1 hour before the end of surgery. After removal of a head holder and application of dressings, inhaled air was discontinued and 100% oxygen was supplied.

Before insertion of a PLMA (ProSeal™), predetermined propofol effect-site concentration was held constant for 10 minutes. Remifentanil was set at 2 ng/ml as target and the concentration was also maintained for the same period as propofol. Return of neuromuscular function was ascertained by four responses of adductor pollicis to TOF stimulation. Following a gentle suctioning of oral cavity, a deflated PLMA was inserted while an endotracheal tube was still in place. The size of a PLMA was selected based on the patient’s weight; size 3 was used for patients of 40-60 kg and size 4 for patients more than 60 kg. The insertion was tried by an experienced anesthesiologist who was unaware of the concentration of propofol. After removal of an endotracheal tube, the cuff of PLMA was inflated and it was connected to the breathing system. The adequacy of ventilation was evaluated by examining an appropriate chest movement and observing a proper waveform of capnogram. Infusion of propofol stopped then, while remifentanil continued until spontaneous respiration returned and tidal volume was considered to be sufficient. In case ventilation was impossible, the patient was excluded from the study and ventilation was assisted through a facemask.

A patient’s response to the endotracheal tube/PLMA exchange was described as ‘successful’ or ‘unsuccessful’. An ‘unsuccessful’ exchange referred to an occurrence of adverse responses such as resistance to mouth opening, coughing, bucking, or gross purposeful movements during the insertion of a PLMA, inflation of a cuff or removal of an endotracheal tube. Airway obstruction as laryngospasm during the manipulation was also included. If a LMA was substituted appropriately for an endotracheal tube without any unfavorable reactions, the exchange was considered ‘successful’. Whether the exchange was successful or not was judged by the anesthesiologist who inserted the LMA and another one also blinded to the dose of propofol. When at least one of them documented adverse responses or evidences of airway obstruction, the exchange was reported to be ‘unsuccessful’. The propofol concentration of each patient was determined by a modification of Dixon’s up-and-down method. The starting target effect-site concentration of propofol was 3.5 μg/ml. If the attempt was proved to be
Table 1. Patients’ Characteristics, Anesthesia Time and Period of Time from an Endotracheal Tube/ProSeal Laryngeal Mask Airway (PLMA) Exchange Till the Removal of LMA

<table>
<thead>
<tr>
<th></th>
<th>mean±SD</th>
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<tbody>
<tr>
<td>Sex (M/F)</td>
<td>10/16</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>41.4±14.8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>66.8±25.5</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161.0±9.1</td>
</tr>
<tr>
<td>Anesthesia time (min)</td>
<td>348.1±117.1</td>
</tr>
<tr>
<td>Period of time from an exchange till the removal of LMA (min)</td>
<td>8.4±5.8</td>
</tr>
</tbody>
</table>

Values are mean±SD.

unsuccessful, the target propofol concentration of the next patient was increased by 0.5 μg/ml; if successful, it was decreased by 0.5 μg/ml. The LMA was removed when the patient was breathing adequately and could respond to verbal commands. The period of time from an endotracheal tube/PLMA exchange till removal of the LMA was recorded. Patients were asked after surgery if they had any recall of the events.

A modified Dixon’s up-and-down method was used to determine the target effect-site concentration (Cet) of propofol required for successful exchange in 50% of patients. The Cet was determined by calculating the mean of the midpoint concentrations of all independent pairs of patients who manifested a crossover from ‘unsuccessful’ to ‘successful’ exchange. It is expressed as mean± standard deviation (SD). We also analyzed our data by a logistic regression model (SPSS for windows 18.0; SPSS Inc., Chicago, IL, USA) to obtain the probability of successful exchange versus target effect-site concentration of propofol, the maximum likelihood estimators of the model parameters and goodness of fit. In this analysis, EC50 and EC95 were defined as the target effect-site concentrations of propofol needed to exchange an endotracheal tube for the PLMA successfully in 50% and 95% of patients, respectively. A p-value <0.05 was considered statistically significant.

Table 2. The Responses of 13 Patients Who Manifested ‘Unsuccessful’ Exchange of an Endotracheal Tube for A PLMA

<table>
<thead>
<tr>
<th>Adverse Response</th>
<th>Number of patients</th>
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<tbody>
<tr>
<td>Resistance to mouth opening</td>
<td>2</td>
</tr>
<tr>
<td>Movement of tongue or lip</td>
<td>4</td>
</tr>
<tr>
<td>Swallowing movement</td>
<td>3</td>
</tr>
<tr>
<td>Coughing</td>
<td>2</td>
</tr>
<tr>
<td>bucking</td>
<td>2</td>
</tr>
<tr>
<td>Gross purposeful movements</td>
<td>1</td>
</tr>
<tr>
<td>Airway obstruction (laryngospasm)</td>
<td>1</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>0</td>
</tr>
</tbody>
</table>

Numbers do not sum up because some patients showed more than one type of response. Values are the number of patients in each category.

Results

The patients’ demographic data, anesthesia time and the period of time from an exchange till the removal of LMA are presented in Table 1.

No patient presented difficulty in mask ventilation or endotracheal intubation. And the PLMA was inserted on the first or second attempt in all of the patients. One patient experienced airway obstruction immediately after the exchange and was recovered after 1 minute. No patient was desaturated below 97%. The responses of patients who manifested ‘unsuccessful’ exchange are summarized in Table 2. None of the patients reported recall of events during anesthesia or surgical procedure.

Employing a modified Dixon’s up-and-down method, the Cet of propofol required to replace the endotracheal tube by an PLMA successfully in 50% of patients was 3.86±0.21 μg/ml (Fig. 1). A logistic regression curve indicating the probability of successful exchange versus concentration of target effect-site concentration of propofol is illustrated in Figure 2. As the figure shows, EC50 and EC95 were 3.75 μg/ml (95% confidence limit, 3.36-4.36 μg/ml) and 4.50 μg/ml (95% confidence limit, 4.11-5.11 μg/ml), respectively. Maximum likelihood estimators of logit model variables in this
Fig. 1. The responses of 26 consecutive patients in whom the exchange of an endotracheal tube for a ProSeal laryngeal mask airway (PLMA) was attempted at different target effect-site concentrations of propofol. Each patient’s data are represented by a circle. Arrows indicate the midpoint concentrations of all independent pairs of patients who manifested crossover from unsuccessful to successful exchange. The target effect-site concentrations (C_{es}) of propofol required to exchange an endotracheal tube for a PLMA successfully in 50% of patients was 3.86 ± 0.21 μg/ml (mean ± standard deviation).

Fig. 2. Dose-response curve plotted from a logistic analysis of individual target effect-site concentrations of propofol and respective responses to the exchange of an endotracheal tube for a ProSeal laryngeal mask airway. The target effect-site concentrations required for a successful exchange in 50% (EC_{50}) and 95% (EC_{95}) of patients were 3.75 μg/ml (95% confidence limit, 3.36-4.36 μg/ml) and 4.50 μg/ml (95% confidence limit, 4.11-5.11 μg/ml), respectively.

Discussion

In recent years, TIVA has been used in increasing numbers of neurosurgical patients. TIVA with propofol and remifentanil allows a predictable titration of anesthesia and a rapid recovery of consciousness and respiration. These characteristics make immediate neurologic examination and early detection of postoperative complications possible. Moreover, propofol has the advantages of increasing cerebral perfusion pressure and decreasing cerebral oxygen consumption and brain swelling.(13-16) It also provides potential neuroprotection by its antioxidant properties.(15) TIVA with propofol and remifentanil is a standard anesthetic technique for elective neurosurgical procedures in our institution, especially due to a rapid return of consciousness. The method of replacing an endotracheal tube by a LMA may be provided a patent airway and alleviated the straining of patients during emergence. (9-12) This technique, however, should be performed under adequate level of anesthesia to prevent coughing, bucking or stress responses caused by the insertion of a LMA, inflation of the cuff or removal of an endotracheal tube.

Takita et al.(17) demonstrated that end-tidal concentrations of sevoflurane for successful exchanges of an endotracheal tube with a LMA in 50% of patients (ED_{50}) and in 95% of patients (ED_{95}) are 2.53% and 2.97%, respectively. The exchange needed a higher end-tidal concentration of sevoflurane than the insertion
of a LMA (ED50: 2.00%) or tracheal extubation (ED50: 1.07%) did. The authors speculated that it may be because the insertion of a LMA, in the presence of an endotracheal tube, stimulates trachea and vocal cords by movement of the tube and the LMA also stimulates upper airway.(17)

We planned this study to determine the effect-site concentration of propofol required for the replacement of an endotracheal tube by a PLMA in neurosurgical patients. Our results suggest that the Cet of propofol required for successful exchange in 50% of patients is $3.86\pm0.21$ μg/ml (a modified Dixon’s up-and-down method). EC50 and EC95 are $3.75$ μg/ml and $4.50$ μg/ml, respectively (a logistic regression method). As for the concentration needed for the insertion of a PLMA, Kodaka et al. showed that the effect-site concentration of propofol to allow the insertion in 50% of patients is $4.32\pm0.67$ μg/ml.(18) Handa-Tsutsui et al. demonstrated that the concentration is $4.9\pm0.20$ μg/ml.(19) Interestingly, the effect-site concentration needed for an exchange is lower than the concentration needed for the insertion of a PLMA in this trial. These findings are not compatible with those of Takita’s article mentioned above. We suppose that the use of remifentanil may explain the lower anesthetic requirement of propofol. The infusion of remifentanil has been continued until the recovery of respiration and consciousness to minimize the influence of wound pain on propofol concentration required for the exchange. A remifentanil plasma or effect-site concentration of 2 ng/mL is considered to provide sedation and analgesia without impeding spontaneous ventilation.(20) Previous reports on the synergic interaction of propofol and remifentanil support this assumption. Some articles have demonstrated a concurrent use of the two drugs showed an additive pharmacodynamic interaction. Their synergic interaction reduced the dose requirements of both agents.(21-23) Grewal K. et al. showed that 0.3 μg/kg of remifentanil, combined with target-controlled infusion of propofol, increased the ease and success rate of LMA insertion with minimal hemodynamic changes.(24) Finally, some researches have shown that a target-controlled concentration of 1 ng/mL remifentanil decreases the MAC of sevoflurane and desflurane for blunting sympathetic responses to surgical incision up to 57% and 60%, respectively.(25,26) From these facts, we can draw the conclusion that remifentanil may interact synergically with propofol and decrease the concentration of propofol needed for the exchange, that is, insertion of a PLMA and removal of the endotracheal tube. Further studies are needed to observe higher concentration of remifentanil can reduce the requirement of propofol further and to find an optimal concentration of remifentanil for providing adequate pain control without interrupting return of consciousness and respiration.

In conclusion, the method of substituting a PLMA for an endotracheal tube may be useful for smooth emergence from general anesthesia. The effect-site concentration of propofol required for successful substitution in 95% of patients undergoing neurosurgical procedures under TIVA is $4.50$ μg/ml. This comparatively low concentration may be explained by the synergic effect of remifentanil and propofol.

**Abstract**

**Purpose:** To determine the target effect-site concentration of propofol required to substitute a ProSeal laryngeal mask airway (PLMA) for an endotracheal tube for providing suitable emergence condition in adult undergoing neurosurgery.

**Methods:** Anaesthesia was maintained with propofol and remifentanil using target controlled infusion (TCI). After end of surgery, predetermined effect-site concentration of propofol (the starting target concentration of
3.5 μg/ml) and remifentanil 2 ng/ml was held for 10 min. A patient’s response to the endotracheal tube/PLMA exchange was described as ‘successful’ or ‘unsuccessful’. The propofol concentration of each patient was determined by a modification of Dixon’s up-and-down method steps by 0.5 μg/ml and concentration for exchange in 50% and 95% patients were obtained by a logistic regression model.

**Results:** The target effect-site concentration of propofol required for successful endotracheal tube/PLMA exchange in 50% of patients was 3.86±0.21 μg/ml and the time from an exchange till the removal of LMA was 8.4±5.8 min.

**Conclusions:** The effect-site concentration of propofol required for endotracheal tube/PLMA exchange in 95% of patients is 4.50 μg/ml.

**Key Words:** Endotracheal tube, Laryngeal masks, Propofol, Target-controlled infusion

**References**

19. Handa-Tsutsui F, Kodaka M. Propofol concentration requirement for laryngeal mask airway insertion was highest with the ProSeal, next highest with the Fastrach, and lowest with the Classic type, with target-controlled infusion. J Clin Anesth 2005;17:344-7.