Comparative effects of thiopentone and propofol on respiratory resistance after tracheal intubation

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Summary

To compare the effects of propofol and thiopentone on tracheal intubation-induced bronchoconstriction, 37 patients were allocated randomly to anaesthesia with either thiopentone 4 mg kg\(^{-1}\) followed by a 15-mg kg\(^{-1}\) h\(^{-1}\) continuous infusion or propofol 3 mg kg\(^{-1}\) followed by a 9-mg kg\(^{-1}\) h\(^{-1}\) continuous infusion. Intubation was facilitated by vecuronium 0.1–0.2 mg kg\(^{-1}\). Respiratory system resistance (R\(_{ts}\)) was measured by a CP-100 pulmonary function monitor, 5 min after intubation. The 5-min post-intubation R\(_{ts}\) values were significantly lower in the propofol group (8.5 (SD 1.5) cm H\(_2\)O litre\(^{-1}\) s\(^{-1}\)) than in the thiopentone group (10.9 (3.2) cm H\(_2\)O litre\(^{-1}\) s\(^{-1}\)). Thirty minutes after commencing isoflurane–nitrous oxide anaesthesia, R\(_{ts}\) declined by 17.5 (SEM 3.6) % from baseline in the thiopentone group, but by only 1.6 (2.6) % in the propofol group. We conclude that the dose of propofol administered provided more protection against tracheal intubation-induced bronchoconstriction than an induction dose of thiopentone. (Br. J. Anaesth. 1996; 77: 735–738)

Key words

Bronchoconstriction may occur after tracheal intubation\(^1\) and occasionally may be severe enough to produce life-threatening decreases in gas flow. Because induction is the period of highest risk for bronchospasm it is important to identify induction agents which minimize the bronchoconstrictor response to tracheal intubation.

The effects of thiopentone on airway resistance remain controversial. Early studies indicated that thiopentone releases histamine and constricts airways.\(^4\) However, thiopentone may also inhibit vagal reflexes,\(^7\) and at higher concentrations produce bronchodilatation.\(^8\) The effects of propofol on human bronchomotor tone are also inconclusive. There are studies reporting bronchospasm during propofol induction\(^9\) but there are also some stating otherwise.\(^10\) Mehr and Linderman, comparing the effects of propofol on peripheral airway responsiveness with the effects of thiopentone and halothane, showed that propofol afforded no benefit over thiopentone or halothane.\(^11\) Cheng and colleagues recently found that in vitro, propofol did not produce smooth muscle relaxation.\(^12\) However, a study comparing the incidence of wheezing in asthmatic patients induced by different i.v. anaesthetic agents found that fewer patients wheezed after receiving propofol compared with a barbiturate.\(^13\)

The purposes of this study were to compare the effects of propofol and thiopentone on tracheal intubation-induced bronchoconstriction and to investigate how the addition of an inhalation anaesthetic further influences bronchomotor tone after intubation.

Patients and methods

This study was carried out with the approval of the Human Subjects Review Board of Chang Gung Memorial Hospital. All patients underwent surgery of the extremities and were of normal body habitus, ASA I or II.

After obtaining informed consent, 37 patients, aged 20–50 yr, were allocated to one of two groups. Induction was performed by an anaesthetist who did not participate in the study. The induction agent chosen was according to a random number design which was not revealed until the start of induction. The anaesthetist recording the resistance measurement was unaware of the medication used for induction. Anaesthesia in the thiopentone group was induced with thiopentone 5 mg kg\(^{-1}\) i.v. There was a variance allowed of 1 mg kg\(^{-1}\) depending on the response of the patient. Vecuronium 0.1–0.2 mg kg\(^{-1}\) was given to facilitate oral tracheal intubation using a 7.5-mm tube. After intubation, an i.v. infusion of thiopentone 15 mg kg\(^{-1}\) h\(^{-1}\) was started immediately to maintain an adequate anaesthetic level until the end of the study. Anaesthesia in the propofol group was induced with 2.5 mg kg\(^{-1}\) and a bolus dose of vecuronium followed by a continuous infusion of propofol 9 mg kg\(^{-1}\) h\(^{-1}\) for maintenance.
of anaesthesia. Patients’ lungs were ventilated with 100% oxygen using a Drager Narkomed II ventilator (North American Drager, PA, USA) at a tidal volume of 650 ml, an inspiratory flow rate of 0.6 litre s$^{-1}$ with a rectangular wave pattern and a ventilatory frequency of 10 bpm. Mean end-tidal $PcO_2$ was 4.6 kPa in the thiopentone and propofol groups. All patients were positioned supine.

Resistance of the respiratory system ($Rs$) was measured 2 and 5 min after intubation with a CP-100 pulmonary function monitor (Bicore, Irvine, CA, USA). The CP-100 pulmonary function monitor is a monitoring device consisting of a flow transducer (VarFlex) and an oesophageal balloon catheter which allows breath-by-breath measurement of tidal volume ($V_T$), airway flow ($V$), transpulmonary pressure (airway – oesophageal pressure) and airway pressure ($Paw$). The flow transducer was connected to the ventilation system between the tracheal tube and the Y-piece. The oesophageal balloon catheter was left exposed to ambient pressure to measure $Rs$. Measurement of $Rs$ was based on pressure and flow measurements in the airway. Resistance measurements were calculated using the isovolume method (the difference in airway pressure divided by the sum of the flows taken at the same volume during both inspiration and expiration)$^{14-17}$ and included resistance of the tracheal tube. The CP-100 monitor is equipped with self-diagnostic hardware tests which perform self-calibration of the measuring system.

After the 5-min period during which the patient received only the induction agent, inhalation anaesthesia was begun with 1.3% isoflurane and 50% nitrous oxide in oxygen, as monitored by end-tidal concentration. Inspirated concentrations of isoflurane were adjusted to 5% initially to achieve this end-tidal concentration as rapidly as possible and were then adjusted using the end-tidal monitor. Respiratory measurements were repeated 30 min after initiation of inhalation anaesthesia.

As secretions in the trachea may affect resistance data, the trachea was suctioned 1 min before every $Rs$ measurement to remove any sputum that might influence the resistance measurement. Suctioning was performed with a 10-ml sputum trap attached between the suction catheter and the vacuum source. The total volume of mucus collected during the study was used to categorize patients post hoc into two groups: mucus producers (>1 ml) and non-mucus producers (<1 ml).

**STATISTICAL ANALYSIS**

Comparisons of differences between groups were made using the two-tailed Student’s $t$ test for unpaired data. Comparisons within groups between different times were made using analysis of variance (ANOVA) and comparisons within subgroups at different times using the Student’s $t$ test for paired data and Bonferroni’s correction to identify specific differences. $P<0.05$ was considered significantly different.

**Results**

Patients were allocated randomly to one of two groups: propofol ($n=19$, mean age 29 (range 20–45) yr) and thiopentone ($n=18$, mean age 33 (20–49) yr) (table 1). Patients with a history of pre-existing chest disease were excluded. There was no correlation between mucus production and smoking.

Two and 5 min after intubation, $Rs$ values were 8.5 ($SD$ 1.5) cm H$_2$O litre$^{-1}$ s$^{-1}$ and 8.5 (1.4) cm H$_2$O litre$^{-1}$ s$^{-1}$ in the propofol group, respectively, but 10.9 (3.2) cm H$_2$O litre$^{-1}$ s$^{-1}$ and 11.0 (3.4) cm H$_2$O litre$^{-1}$ s$^{-1}$ in the thiopentone group (fig. 1) ($P<0.01$, Student’s $t$ test for the effect of the drug).

Thirty minutes after initiation of isoflurane–nitrous oxide anaesthesia, $Rs$ had declined significantly (to 8.6 (SEM 1.3) cm H$_2$O litre$^{-1}$ s$^{-1}$; $P<0.001$, Student’s $t$ test paired data comparing $Rs$ after intubation and 30 min after inhalation anaesthesia) by a mean of 17.5 (3.6) % in the thiopentone group ($P<0.01$) compared with after intubation, but had declined (to 8.3 (1.0) cm H$_2$O litre$^{-1}$ s$^{-1}$; $P<0.002$, Student’s $t$ test) by only 1.6 (2.6) % in the propofol group (fig. 2) ($P<0.001$ for percentage decline of thiopentone vs propofol). $Rs$ in the propofol group 30 min after initiation of inhalation anaesthesia did not differ from $Rs$ after intubation.

In our 37 patients there was a clear difference in $Rs$ between mucus and non-mucus producers. $Rs$

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Table 1  Patient data (mean ($SD$ or range)). No significant differences between groups

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>Mucus producers</th>
<th>Non-mucus producers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>No of patients</td>
<td>Age (yr)</td>
</tr>
<tr>
<td>Thiopentone</td>
<td>7 (5 male; 3 smokers)</td>
<td>37.5 (26–49)</td>
</tr>
<tr>
<td>Propofol</td>
<td>5 (5 male; 4 smokers)</td>
<td>33.8 (24–45)</td>
</tr>
</tbody>
</table>
of mucus producers was significantly higher than non-mucus producers (Student’s t test for unpaired, \( P<0.01 \)) (table 2). Rs values were consistently high regardless of sputum volume among mucus producers suggesting that mucus production is a marker for hyper-reactivity in our patients.

**Discussion**

The important findings of this study were that compared with thiopentone, propofol attenuated the intubation-induced bronchoconstrictive response. Mucus production was a marker of airway reactivity. In patients with normal airways, propofol provided protection against the intubation-induced bronchoconstrictive response equivalent to 30 min administration of end-tidal 1.3% isoflurane–50% nitrous oxide anaesthesia. In mucus-producing patients however, propofol did not provide full protection but was still better than thiopentone.

We chose to use vecuronium because of the lack of histamine release,\(^{18}\) and the lack of drug interaction between vecuronium and propofol.\(^{19}\)

The isovolume method of measuring respiratory resistance used in this study includes the resistance of the tracheal tube. At the flow rates used with a 7.5-mm tracheal tube, this would have resulted in a consistent overestimation of resistance of approximately 4 cm H\(_2\)O litre\(^{-1}\) s\(^{-1}\).\(^{14}\) While the exact effect of the tracheal tube on the value depends on expiratory flows and would vary slightly from patient to patient, inter-patient variation would be very small. If the value of 4 is subtracted from all patients, the mean values for the propofol and thiopentone groups become 5 and 7 cm H\(_2\)O litre\(^{-1}\) s\(^{-1}\), suggesting an approximate 40% increase in resistance if thiopentone is used for induction.

Although the Bicore pulmonary function monitor provides measurements of the resistance of the lung \((R_L)\), Rs was used to study the response because of its reproducibility and simplicity of measurement, requiring only airway pressure and flow data. Supine position may influence oesophageal pressure readings and decrease accuracy, and technical difficulties because of oesophageal secretions and catheter movement may make measurements of \(R_L\) less reproducible. Under anaesthesia and neuromuscular paralysis, there is a correlation of 0.9998 between \(R_L\) and Rs in rabbits.\(^{20}\) Given the inherent difficulties of the oesophageal catheter, Rs provides more reliable data. Therefore, we left the oesophageal catheter port of the Bicore open to air so that we measured Rs.

Our results suggesting a beneficial effect of propofol on the airways are consistent with several recent studies. Pizov and co-workers showed that the incidence of wheezing was significantly greater in asthmatic patients receiving a barbiturate for induction of anaesthesia than in patients receiving propofol.\(^{21}\) However, they made no measurement of respiratory resistance. Cigarini and colleagues demonstrated that propofol prevented fentanyl-induced bronchoconstriction in surgical patients.\(^{21}\) Pederson anecdotally reported that sedative doses of propofol inhibited postoperative bronchospasm in two patients with hyper-reactive airway disease.\(^{22}\) Prien demonstrated that moving patients from the
supine to the lithotomy position, airway impedance was unchanged for patients anaesthetized with propofol, but it increased significantly for patients anaesthetized with thiopentone. Our objective findings after airway stimulation provide further evidence of a protective effect of propofol.

A secondary finding of the study was that a subgroup of patients had significant mucus production after intubation, and that the greatest increase in respiratory resistance occurred in this group of patients. Our finding agrees with others as mucus production has been shown previously to be a marker of airway irritation. Production of 1 ml represents 10% of the normal daily production of the airways and appears to have been a marker for patients with more reactive airways. Among mucus producers, Rs 5 min after intubation was significantly higher in the thiopentone group than in the propofol group suggesting that propofol is significantly better than thiopentone in providing protection against the increase in airway resistance in these patients with more reactive airways.

Our finding that there was no correlation between mucus production and smoking agrees with the results in our previous study on the effects of fenoterol on the airway resistance response to tracheal intubation. Inhalation anaesthetics have been shown to cause bronchodilatation in a dose-related manner. Our results in the thiopentone mucus and non-mucus producers confirmed this effect. The addition of end-tidal concentrations of 1.3% isoflurane–50% nitrous oxide after propofol produced a further slight decrease in the mucus producers (significant difference P=0.049 for two-tailed and 0.025 for one-tailed), but not in the non-mucus producers, suggesting that propofol provides bronchodilatation almost equivalent to that provided by inhalation anaesthetics. However, as the number of mucus producers studied was relatively small, interpretation of the decrease in Rs 30 min after inhalation anaesthesia for the propofol mucus producers must be made with caution. The magnitude of the additional bronchodilatation after isoflurane was relatively small, implying that even in mucus producers, propofol produced substantial protection.

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References