

Original Article

Assessment of tracheal intubation in adults after induction with sevoflurane and different doses of propofol: a randomly controlled trial

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Abstract: Intubation without prior administration of muscle relaxants is a common practice in children and adults with potential difficult airways. We aimed to investigate the effects of adding different doses of propofol on tracheal intubation and the time to return of spontaneous breathing during inhalation induction of patients. 150 patients undergoing operations were randomly given propofol IV at 1.0, 1.5 and 2.0 mg/kg (namely 1.0-propofol, 1.5-propofol and 2.0-propofol, respectively) after inhalational induction with sevoflurane. Tracheal intubating conditions, time to return of spontaneous breathing, postoperative hoarseness, end-tidal carbon dioxide concentration ($P_{ET}CO_2$), and pulse oxygen saturations (SpO_2) were assessed. Tracheal intubation was successful in all patients. Intubating conditions were acceptable in 31/50, 42/50 and 47/50 in those subjects given propofol 1.0, 1.5 or 2.0 mg/kg, respectively. Intubation scores were similar in groups 1.5-propofol and 2.0-propofol, and were significantly higher than in group 1.0-propofol ($P = 0.013$). Time to return of spontaneous breathing in group 2.0-propofol was significantly prolonged compared with groups 1.5-propofol and 1.0-propofol (197.0 ± 49.4 sec vs. 130.4 ± 32.7 sec, $P < 0.001$; 197.0 ± 49.4 sec vs. 104.8 ± 22.6 sec, $P < 0.001$, respectively). SpO_2 in group 2.0-propofol was significantly lower than group 1.0-propofol and 1.5-propofol. However, $P_{ET}CO_2$ in group 2.0-propofol was significantly higher than in groups 1.0-propofol or 1.5-propofol. Propofol at a dose of 1.5 mg/kg provides intubating conditions similar to propofol at 2.0 mg/kg in patients. Time to return of spontaneous breathing followed by a dose of 1.5 mg/kg propofol was significantly shorter than that followed by a dose of 2.0 mg/kg propofol.

Keywords: Sevoflurane, propofol, tracheal intubation, time to resumption of spontaneous breathing

Introduction

Sevoflurane is a non-irritating inhalational anesthetic agent with low blood gas solubility [1] and less interference to respiration and has been used for anesthesia induction in difficult airways [2, 3]. However, induction only by sevoflurane for tracheal intubation cannot provide satisfactory intubating conditions in short time, and which accompanied with acute hemodynamics changes when intubation [1, 4]. There are investigations on the effect of combining sevoflurane with adjuvant medications including depolarizing neuromuscular blockers [4] and opioids [5-7]. While they provide suitable conditions, their use may be followed by a long time to return of spontaneous breathing (RSB) and chest muscle rigidity, and thus, might be a

huge risk for patients with difficult airways if ventilation cannot be assisted. It has been found that the combination of sevoflurane/propofol can provide a relaxation of oropharyngeal muscles [8], a rapid RSB and a deeper level of anesthesia for children intubation [9-11]. We hypothesized that an appropriate dose of propofol in combination with sevoflurane could provide acceptable intubating condition and a shorter time to RSB without using neuromuscular blocking agents in adults, too.

Patients and methods

After obtaining the approval from West China Hospital Ethics Committee (registration number: ChiCTR-TRC-12002795) and written informed consent from each participant, we

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Table 1. Assessment and classification of intubation conditions

	Excellent	Good	Poor
Ease of laryngoscopy	Ease	Fair	Difficult
Vocal cord position	Abducted	Intermediate	Closed
Vocal cord movement	None	Moving	Closing
Airway reaction	None	Diaphragm	Sustained > 10 s
Movement of limbs	None	Slight	Vigorous

Excellent = all criteria are excellent, Good = all criteria are excellent or good, Poor = any criterion is poor.

Table 2. Patient characteristics

	1.0-propofol	1.5-propofol	2.0-propofol
Age (yr)	40.4 ± 7.2	42.1 ± 9.3	40.4 ± 8.9
Sex ratio (M/F)	26/24	25/25	28/22
Weight (kg)	61.3 ± 9.5	62.4 ± 9.5	59.2 ± 8.4
Height (cm)	163.1 ± 6.9	162.7 ± 7.0	161.3 ± 7.5
Time to LOC (s)	72.1 ± 15.0	70.6 ± 14.9	70.1 ± 18.1
C _{ET} SEV (%)	5.1 ± 0.5	5.1 ± 0.5	5.1 ± 0.4
Intubation time (s)	29.9 ± 8.2	30.3 ± 7.4	29.8 ± 6.1
Time to RSB (s)	104.8 ± 22.6	130.4 ± 32.7	197.0 ± 49.4 ^{*,*}
P _{ET} CO ₂ after RSB	27.8 ± 6.8	28.8 ± 6.3	32.2 ± 5.3 ^{*,*}
SpO ₂ after RSB	97.7 ± 1.7	97.4 ± 1.7	95.5 ± 2.4 ^{*,*}

LOC = loss of consciousness. C_{ET}SEV = end tidal concentration of sevoflurane; RSB = return of spontaneous breathing. P_{ET}CO₂ = end-tidal carbon dioxide concentration; SpO₂ = pulse oxygen saturations. Values are median and range or mean ± SD or median (range). *P < 0.05 versus group 1.0-propofol. [#]P < 0.05 versus group 1.5-propofol.

studied 150 adult patients, ASA I-II, aged 18-55 years, who presented for elective surgery and required tracheal intubation were studied. Patients with sleep apnea for obesity or with a history of oesophageal reflux and asthma, allergic reaction to any of the study drugs, predictive signs of difficult intubation were excluded.

The enrolled patients were randomly allocated into three groups using a computer-generated random number: three groups were given propofol IV at 1.0, 1.5 and 2.0 mg/kg (namely 1.0-propofol, 1.5-propofol and 2.0-propofol, respectively) administered depending on actual body weight. No premedication was given. On arrival in the operating room, the standard monitoring devices (electrocardiogram, pulse oximeter, and non-invasive blood pressure) were applied. All patients were pre-oxygenated for 3 min with 100% oxygen through a tightly-fitting mask and then connected to a semi-closed anesthetic circuit prefilled with 8% sevoflurane. Fresh gas flow rate was set at 6 L/min.

Patients were asked to hold the vital capacity breath for as long as possible. If necessary, a second breath was taken. While holding their breaths, patients were asked to open their eyes every 10 seconds, failure to do so was defined as loss of consciousness (LOC). When LOC was firmly established, the positive control ventilation was applied to maintain end-tidal carbon dioxide pressure (P_{ET}CO₂) between 30-40 mmHg. Two minutes later, three randomly divided groups were given propofol for 30 seconds at dose of 1.0, 1.5 or 2.0 mg/kg, respectively. Laryngoscopy and intubation using a cuffed tube (7.5[#] for man or 7.0[#] for women) were performed 60 s after propofol administration. An investigator blinded to the treatments performed all laryngoscopies and graded the intubating conditions. Intubation time was calculated from the start to the end of a successful intubation, and intubating conditions were evaluated as proposed and shown

in **Table 1** [12]. Both good and excellent intubating conditions were regarded as acceptable whereas the poor one was regarded as unacceptable. After orotracheal intubation, patients' airway was left unsupported, the time to RSB was determined by obviously recognizable end-tidal CO₂ waveforms appeared on the monitor followed by diaphragm movement. Depth of anesthesia was adjusted and ventilation was controlled mechanically on recovery of spontaneous breathing. If tracheal intubation failed, an additional dose of 1 mg/kg propofol plus succinylcholine was given for another intubation. Patient who failed intubation was identified as the poor intubation condition. The followed up data was not recorded.

Demographic data including patients' age, height and weight were collected. The end-tidal sevoflurane concentration (C_{ET}SEV) before intubation, intubating conditions, the time to LOC, intubation time and time to RSB were also recorded. P_{ET}CO₂ and pulse oxygen saturations

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Table 3. Intubation conditions

	Score distribution (excellent-good-poor)		
	1.0-propofol	1.5-propofol	2.0-propofol
Ease of laryngoscopy	20-24-6	30-20-0	38-22-0
Vocal cord position	18-22-10	28-22-0	30-20-0
Vocal cord movement	21-25-4	29-27-4	32-17-1
Airway reaction	5-26-19	17-25-8	22-25-3
Movement of limbs	22-23-5	40-10-0	45-5-0
Overall conditions	12-19-19	17-25-8	22-25-3

Table 4. Hemodynamic changes

	1.0-propofol	1.5-propofol	2.0-propofol
SBP (mmHg)	--	--	--
Baseline	115.2 ± 9.0	114.9 ± 7.7	115.7 ± 9.0
Preintubation	111.1 ± 12.5	113.0 ± 11.4	113.0 ± 8.2
Postintubation	120.4 ± 15.1 [#]	120.2 ± 10.1 [#]	111.5 ± 12.0 ^{a,b}
RSB	117.4 ± 11.9	114.0 ± 13.7	110.8 ± 8.8 ^a
HR (bpm)	--	--	--
Baseline	79.4 ± 10.4	77.4 ± 10.9	76.8 ± 8.6
Preintubation	85.0 ± 11.6 [*]	84.3 ± 11.9 [*]	83.4 ± 12.9 [*]
Postintubation	90.1 ± 8.2 ^{*,#}	85.9 ± 8.8 ^{*,a}	82.9 ± 9.9 ^{*,a}
RSB	87.7 ± 8.7 [*]	83.4 ± 10.8 ^{*,a}	81.9 ± 8.0 ^a

Values are mean ± SD. 1.0-propofol = propofol 1.0 mg/kg; 1.5-propofol = propofol 1.5 mg/kg; 2.0-propofol = propofol 2.0 mg/kg. RSB: return of spontaneous breathing. ^{*}P < 0.05 versus baseline values. [#]P < 0.05 versus preintubation values. ^aP < 0.05 versus group 1.0-propofol. ^bP < 0.05 versus group 1.5-propofol.

Table 5. Assessment of postoperative hoarseness

	Grade 0	Grade 1	Grade 2	Grade 3
1.0-propofol	20 (40%)	20 (40%)	10 (20%)	0 (0%)
1.5-propofol	30 (60%) [*]	15 (30%)	5 (10%)	0 (0%)
2.0-propofol	40 (80%) ^{*,#}	8 (16%)	2 (4%)	0 (0%)

Values are shown as numbers of patients, n (%). Grade 0 = no hoarseness; 1 = noticed by patient, 2 = obvious to observer, 3 = aphonia. ^{*}P < 0.05 versus group 1.0-propofol. [#]P < 0.05 versus group 1.5-propofol.

(SpO₂) were recorded when the spontaneous breathing resumed. The systolic blood pressure (SBP) and heart rate (HR) were recorded before induction (baseline), 1 minute before the laryngoscopy (pre-intubation), 1 minute after the intubation (post-intubation) and when spontaneous breathing returned. During recovery, in the post-anesthetic care unit, patients' satisfaction to the anesthesia and intraoperative awareness were assessed by an anesthetist who was blinded to the procedures. Furthermore, the anesthetist assessed the postoperative hoarseness (PH) as the follows: 0 = none (no hoarseness), 1 = noticed by patient, 2 =

obvious to observer and 3 = aphonia [13].

Statistic analysis

Sample size was calculated in expectation of 90% acceptable intubating condition rate in group 2.0-propofol and a 40% reduction of the acceptable intubating condition rate in the group 1.0-propofol. Type 1 error was set to 5% and type 2 error was set to 10%. With this assumption, 30 patients were required per group. Statistical analyses were performed using PASW Statistics 18 (SPSS Inc.). Data were expressed as median (range), or means ± standard deviation (SD), or number of patients (%). Intubating conditions, postoperative hoarseness, gender were analyzed using Chi-square test. The time to LOC, C_{ET}SEV, intubation time, time to RSB and P_{ET}CO₂ were compared using one-way ANOVA. Changes in HR and SBP were analyzed using repeated measures ANOVA. The SpO₂ values when the spontaneous ventilation resumed were evaluated using Kruskal-Wallis Test. P < 0.05 was considered statistically significant.

Results

No patient was lost to follow-up and all patients completed the study. Patients' characteristics did not differ significantly and there were no significant differences in time to LOC, intubation time and the C_{ET}SEV pre-intubation among three groups (Table 2). No complications such as laryngospasm, bronchial spasm and gastric aspiration were observed.

Tracheal intubating conditions

Tracheal intubation was accomplished successfully in each patient and no patient was given an extra dose of propofol and succinyl-

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choline. Excellent intubating conditions were 24%, 34% and 44% of patients in groups 1.0-propofol, 1.5-propofol and 2.0-propofol, respectively. Good intubation conditions were seen in 19 (38%, propofol 1.0 mg/kg), 25 (50%, 1.5 mg/kg), and 25 (50%, 2.0 mg/kg) patients. Poor intubation conditions were seen in 19 (38%, propofol 1.0 mg/kg), 8 (16%, 1.5 mg/kg), and 3 (6%, 2.0 mg/kg) patients (**Table 3**). Thus, intubation scores of patients in 1.0-propofol was significantly lower than that in 1.5-propofol and 2.0-propofol ($P = 0.013$, $P = 0.000$). However, there was no significant difference between groups 1.5-propofol and 2.0-propofol ($P = 0.11$).

Time to return of spontaneous breathing

The time to return of spontaneous breathing of patient in group 2.0-propofol was significantly longer than that in 1.5-propofol and 1.0-propofol ($P = 0.000$, $P = 0.000$), and significant difference was noted between 1.5-propofol and 1.0-propofol ($P = 0.001$). When spontaneous breathing resumed, $P_{ET}CO_2$ were similarly in groups given 1.0 mg/kg and 1.5 mg/kg, and were significantly lower than group given 2.0 mg/kg ($P = 0.001$, $P = 0.007$). In contrast, SpO_2 of patients given 1.0 mg/kg and 1.5 mg/kg propofol were significantly higher than patients given 2.0 mg/kg ($P = 0.000$, $P = 0.000$). One patient in 2.0-propofol developed a mild hypoxemia (88% O_2 saturation), but this was quickly resolved with assisted respiration.

Cardiovascular responses

Cardiovascular responses to the induction and intubation were shown in **Table 4**. Decreased mean SBP was seen before intubation compared with the baseline values in all groups, but SBP increased significantly after intubation in groups 1.0-propofol and 1.5-propofol ($P < 0.05$). The mean HR increased significantly after the induction and remained significantly faster than baseline values after tracheal intubation in all groups during the investigation ($P < 0.05$). There were no significant differences in mean HR and SBP among the groups at any time point.

Postoperative hoarseness

During recovery, no patients had any memory about surgery and anesthesia after LOC. They

were satisfied with the anesthesia regime and the sevoflurane induction. No aphonia was found in all patients. As shown in the **Table 5**, the patients with laryngeal complication in 1.0-propofol were fewer than that in 2.0-propofol.

Discussion

This study aimed to determine the optimal dose of propofol in combination with 8% sevoflurane to provide acceptable intubating conditions and the minimal time to RSB in ASA I-II adults. We found that there was an increase in the percentage of overall excellent intubating conditions following the increasing dose of propofol and that 2 mg/kg propofol provided superior intubating conditions but prolonged the time to RSB as compared with those of 1.0 and 1.5 mg/kg. Propofol at 1.5 mg/kg not only provided clinically acceptable tracheal intubating conditions, but also made patients to return to spontaneous breathing before a critical oxyhemoglobin desaturation.

It has been reported that in young non-premedicated adult patients, the time to achieve acceptable tracheal intubating conditions with 6-7% sevoflurane is 6.4 min [14]. In our study, the patients continuously inhaled 8% sevoflurane for about 4.7 min accompanied with propofol and most patients achieved clinically acceptable intubating conditions. The combination of sevoflurane and propofol may cause synergistic effects on sedation and muscle relation. Therefore, propofol shortened the time to achieve acceptable tracheal conditions and improved tracheal intubation conditions. The $C_{ET}SEV$ required for tracheal intubation (MAC_{EI}) in adults is 4.52% and the ED_{95} is 8.07% [1]. Therefore, the inhalation sevoflurane concentration was set at 8%, when tracheal intubation the mean $C_{ET}SEV$ was 5.1% in our study. Jo et al. showed that when being used in combination with end-tidal concentration of 3%-4% sevoflurane, based on the Dixon's up-and-down method, 1-2 mg/kg propofol provided excellent intubating conditions in children [9]. And the study by Siddk-Sayyid et al. showed that propofol at 2 mg/kg was superior to that of propofol at 1 mg/kg for tracheal intubation in children during 8% sevoflurane induction [11]. Owing to the fact that the dose of anesthetics required for adults is lower than that required for children, we chose propofol at the doses of 1-2 mg/kg in combination with 8% sevoflurane in this study.

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Time to the return of spontaneous breathing followed by succinylcholine and thiopental in adults were reported 7.0 and 4.1 min, which were longer than that observed in our study [15]. However, time to RSB after being given remifentanyl (4 ug/kg) and propofol (2 mg/kg) in children was noted 6.4 min [16], while studies in adults showed a shorter time to RSB (up to 6.1 min) for remifentanyl doses up to 2 ug/kg [17]. Therefore, our study has shown that propofol/sevoflurane combination could shorten the time to return of spontaneous breathing, but which was longer than that induced by sevoflurane or propofol alone [18]. Although an initial spontaneous breathing may not reflect a completely functional recovery, this may still prevent hemoglobin desaturation whether or not the patient remained sedation.

We found that patients got acceptable intubation conditions were 84% and 94% in group 1.5-propofol and 2.0-propofol, even with 1.0 mg/kg propofol and 8% sevoflurane induction, it was up to 62% in our study. Compared with that reported by Joo et al. intubating conditions were acceptable in 89% and 54% in subjects administered with remifentanyl at 2 or 1 ug/kg and 8% sevoflurane [5]. But another similar study found the percentage of patients got acceptable conditions was 100% [19]. Bradycardia, hypotension and a longer time to return of spontaneous breathing were noted in these studies with remifentanyl for induction. However, in another study in adults, acceptable intubating conditions were observed in 66.7%-100% patients given with succinylcholine and propofol, indicating that relaxants could improve the intubating conditions [20]. Our study has shown that sevoflurane/propofol combination without relaxants could provide the acceptable intubating conditions, which are similar to other proposal without relaxant. Therefore, when there is a contraindication to neuromuscular blocking drug, propofol/sevoflurane combination may provide the alternative induction program. Considering the items of the observational intubation score, ease of laryngoscopy, vocal cord position, vocal cord movement and airway reaction, especially the airway reaction, contributed to the differences in acceptable tracheal intubation conditions between groups. Thus, the topical anesthesia to the larynx and trachea before intubation may decrease the reactions to laryngoscopy and

tracheal intubation. Even if in the group 1.0-propofol, most patients could be easily laryngoscoped to expose their vocal cord. Thus, a low dose of propofol in combination with sevoflurane maybe used for laryngoscopy in subsequent research.

The incidence of laryngeal morbidity the quality was affected by tracheal intubation conditions, which has been reported [13]. Consequently, we assessed PH and the results showed that patients with laryngeal complication were significantly more than in group 1.0-propofol. The PH results are related to the tracheal intubation conditions, especially to the airway reactions. The quality of intubation condition contributes to laryngeal complication, and improving tracheal intubation condition is urgently needed when tracheal intubation is performed without muscle relaxants. But only 80% of patients without any laryngeal complication were seen in 2.0-propofol, maybe the action of tracheal intubation and the retained endotracheal tube itself lead to this morbidity. Thus, gentle operation and strengthened management during retaining the endotracheal tube are strongly needed.

We acknowledge that this study had several limitations. Firstly, no normal participants were enrolled as the control group and studied. Since it has been known that induction by sevoflurane alone for tracheal intubation in adults is accompanied with many adverse complications. Secondly, we did not monitor the bispectral values during the experiment and thus, could not assess the anesthetic depth of patients. Furthermore, this regimen for tracheal intubation was not recommended to the elderly or the hemodynamically compromised patients and was a contraindication to patients with full stomach.

In conclusion, propofol at a dose of 1.5 mg/kg provide intubation conditions similar to propofol at 2.0 mg/kg in patients. Time to return of spontaneous breathing followed by a dose of 1.5 mg/kg propofol was significantly shorter than that followed by a dose of 2.0 mg/kg propofol.

Disclosure of conflict of interest

None.

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