Propofol is superior to thiopental for intubation without muscle relaxants

[Le propofol est supérieur au thiopental pour l'intubation sans myorelaxants]

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Purpose: To compare intubating conditions and cardiovascular changes following induction of anesthesia and tracheal intubation in patients receiving either lidocaine-remifentanil-propofol or lidocaine-remifentanil-thiopental prior to induction.

Methods: In a randomized, double-blind study 76 healthy adult patients were assigned to one of two groups: lidocaine 1.5 mg·kg^{-1}, remifentanil 2 μg·kg^{-1} and propofol 2 mg·kg^{-1} (Group P) or lidocaine 1.5 mg·kg^{-1}, remifentanil 2 μg·kg^{-1} and thiopental 5 mg·kg^{-1} (Group T). Ninety seconds after the administration of the hypnotic agent, laryngoscopy and tracheal intubation were attempted. Intubating conditions were assessed as excellent, good or poor on the basis of ease of ventilation, jaw relaxation, position of the vocal cords, and patient's response to intubation and slow inflation of the tracheal cuff. The mean arterial pressure (MAP) and heart rate (HR) were measured 45 sec after hypnotic agent administration, immediately after tracheal intubation, two and five minutes after intubation.

Results: Excellent intubating conditions were obtained in 84% of Group P patients and 50% of Group T patients ($P < 0.05$). The percentage decrease from baseline MAP was significantly higher in Group P than in Group T postinduction (27.4% ± 11.6 *vs* 21.8% ± 10.0) and immediately postintubation (19.0% ± 16.7 *vs* 11.2% ± 14.9). The percentage change from baseline HR was significantly higher in Group P than in Group T postinduction (13.8% ± 9.7 *vs* 0.5% ± 12.4), immediately postintubation (8.7% ± 13.7 *vs* 2.1% ± 13.1), and two minutes postintubation (7.04% ± 14.3 *vs* 3.5% ± 14.3).

Conclusion: Lidocaine-remifentanil-propofol is superior to lidocaine-remifentanil-thiopental for tracheal intubation without muscle relaxants. However, it induces more hypotension and bradycardia.

Objectif : *Comparer les conditions d'intubation et les changements cardiovasculaires suivant l'induction de l'anesthésie et l'intubation endotrachéale chez les patients qui reçoivent un mélange de lidocaïne-rémifentanil-propofol ou de lidocaïne-rémifentanil-thiopental avant l'induction.*

Méthode : *Lors d'une étude randomisée et en double aveugle, 76 adultes sains répartis en deux groupes ont reçu : 1,5 mg·kg^{-1} de lidocaïne, 2 μg·kg^{-1} de rémifentanil et 2 mg·kg^{-1} de propofol (Groupe P) ou 1,5 mg·kg^{-1} de lidocaïne, 2 μg·kg^{-1} de rémifentanil et 5 mg·kg^{-1} de thiopental (Groupe T). La laryngoscopie et l'intubation endotrachéale ont été tentées 90 s après l'administration de l'agent hypnotique. Les conditions d'intubation ont été évaluées comme excellentes, bonnes ou pauvres fondées sur la facilité à ventiler, le relâchement de la mâchoire, la position des cordes vocales et la réaction du patient à l'intubation et au gonflement lent du ballonnet trachéal. La tension artérielle moyenne (TAM) et la fréquence cardiaque (FC) ont été mesurées 45 s après l'administration de l'agent hypnotique, immédiatement après l'intubation endotrachéale, deux et cinq minutes après l'intubation.*

Résultats : *Des conditions d'intubation excellentes ont été obtenues chez 84 % des patients du Groupe P et 50 % du Groupe T ($P < 0,05$). La TAM a été significativement réduite par rapport aux mesures de base, davantage dans le Groupe P que dans le Groupe T après l'induction (27,4 % ± 11,6 vs 21,8 % ± 10,0) et immédiatement après l'intubation (19,0 % ± 16,7 vs 11,2 % ± 14,9). La FC a été modifiée par rapport aux mesures de base, plus dans le Groupe P que dans le Groupe T après l'induction (13,8 % ± 9,7 vs 0,5 % ± 12,4), immédiatement après l'intubation (8,7 % ± 13,7 vs 2,1 % ± 13,1) et deux minutes après l'intubation (7,04 % ± 14,3 vs 3,5 % ± 14,3).*

Conclusion : *Le mélange de lidocaïne-rémifentanil-propofol est supérieur à celui de lidocaïne-rémifentanil-thiopental pour l'intubation endotrachéale sans myorelaxants. Cependant, il induit plus d'hypotension et de bradycardie.*

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RECENT studies have suggested that propofol in combination with short-acting opioids such as remifentanil and alfentanil may provide adequate conditions for laryngoscopy and tracheal intubation without using muscle relaxants.[1–8] Such a technique may be used whenever neuromuscular block is not required to facilitate surgical access or when neuromuscular blocking agents are contraindicated.

The addition of lidocaine one to three minutes before intubation has been shown to blunt cough reflexes and dysrhythmias,[9] and hence lidocaine may be used to improve intubating conditions and to minimize the associated hemodynamic changes.[2] Using a randomized double-blind design in healthy adult patients undergoing elective surgery, we compared the intubating conditions and cardiovascular changes following induction of anesthesia and tracheal intubation in patients receiving the combination of *iv* lidocaine 1.5 mg·kg^{-1}, remifentanil 2 μg·kg^{-1} and propofol 2 mg·kg^{-1} *vs iv* lidocaine 1.5 mg·kg^{-1}, remifentanil 2 μg·kg^{-1} and thiopental 5 mg·kg^{-1}.

Methods

After obtaining approval from the Ethics Committee and written informed consent from patients, we studied 76 ASA I–II patients, aged 16 to 60 yr scheduled for elective surgery. Exclusion criteria included a history of hypertension, asthma, drug or alcohol abuse, cardiovascular disease, gastroesophageal reflux, body mass index > 30 kg·m^{-2} and predicted difficulty of intubation.

In the operating room, *iv* access was established by inserting a 20-gauge cannula into a vein in the dorsum of the hand. Midazolam 0.03 mg.kg^{-1} was given intravenously five minutes before induction of anesthesia. Patients received a lactated Ringer's solution 5 mL·kg^{-1} before induction of anesthesia and were randomly assigned, by using a computer-generated table of random numbers, to one of two groups. Both groups received lidocaine 1.5 mg·kg^{-1}, remifentanil 2 μg·kg^{-1} followed by either propofol 2 mg·kg^{-1} (Group P) or thiopental 5 mg·kg^{-1} (Group T). The remifentanil syringe was prepared in a total volume of 10 mL with 0.9% saline. An opaque tape was applied to the syringe containing the hypnotic agent to mask its colour. The syringes were prepared by a nurse who did not take part in the study. Injection of the drugs was performed by an anesthesiologist hidden by a drape so that the anesthesiologist performing the intubation was blinded to the hypnotic used.

All patients were monitored by non-invasive blood pressure monitoring, electrocardiogram, peripheral pulse oximetry and capnometry. Baseline heart rate (HR) and mean arterial pressures (MAP) were recorded. After preoxygenation for two minutes, lidocaine was administered over five seconds followed by a bolus dose of remifentanil over 30 sec and either propofol or thiopental over 20 sec. When the patient became unconscious, as evidenced by loss of eyelash reflex, mask ventilation with 100% oxygen was started. Ninety seconds after hypnotic administration, laryngoscopy and tracheal intubation were attempted by using a Macintosh 3 laryngoscope blade and a 7.0 or 8.0 mm endotracheal tube for females and males respectively.

The ease of mask ventilation and laryngoscopy, jaw relaxation, vocal cord position, and patient response to tracheal intubation as well as to slow (five seconds) inflation of the tracheal cuff (coughing, limb movement) were assessed by the intubating anesthesiologist. The various criteria used for intubating conditions are presented in Table I. These criteria were used to score overall conditions of intubation as excellent (all criteria scored as 1), good (mask ventilation scored as 1 and the other criteria as 1 or 2) or poor (one of the criteria scored as 3). Patients who could not be intubated at the first attempt were given rocuronium 0.6 mg·kg^{-1} *iv* to facilitate tracheal intubation. Anesthesia was maintained with 66% nitrous oxide in oxygen and sevoflurane 0.5% (end-tidal).

Measurements of HR and MAP were performed 45 sec after propofol or thiopental was given (postinduction), immediately after tracheal intubation (postintubation), and two and five minutes after intubation. Ephedrine 6 mg *iv* was given if MAP was reduced to more than 25% of baseline for 60 sec and atropine 200 μg·kg^{-1} was given if HR was less than 50 beats·min^{-1}.

In a previous report using a combination of remifentanil and propofol for tracheal intubation without muscle relaxant, the incidence of excellent intubating condition was approximately 70%.[6] Based on these data and to detect an absolute difference of 20% between the proportions of excellent intubating conditions with 80% power and 0.05 level of significance, 32 patients were required in each group. Data were expressed as mean ± SD. Statistical analysis was performed with Student's t test, Chi-square, or Fisher's exact test as appropriate. $P < 0.05$ was considered statistically significant.

Results

There were no demographic differences between the two groups (Table II). All patients could be ventilated via a facemask after induction of anesthesia and no patient had clinically significant rigidity. The various

TABLE I Scoring criteria at induction and tracheal intubation

Score	*1*	*2*	*3*	*4*
Mask ventilation	Easy	Difficult	Impossible	–
Group P	38	0	0	
Group T	38	0	0	
Jaw relaxation	Complete	Slight tone	Stiff	Rigid
Group P	38	0	0	0
Group T	33	5	0	0
Laryngoscopy	Easy	Fair	Difficult	Impossible
Group P	38	0	0	0
Group T	38	0	0	0
Vocal cord position	Open	Moving	Closing	Closed
Group P	35	1	1	1
Group T	33	0	1	4
Coughing	None	Slight	Moderate	Severe
Group P	33*	2	1	0
Group T	24	6	2	1
Limb movement	None	Slight	Moderate	Severe
Group P	38	0	0	0
Group T	38	0	0	0

Group P = lidocaine-remifentanil-propofol; Group T = lidocaine-remifentanil-thiopental. *$P < 0.05$ *vs* Group T.

TABLE II Patient characteristics

Group (n = 38/group)	*Age (yr)*	*Weight (kg)*	*Sex (m/f)*
Group P	32.6 ± 11.4	69.8 ± 14.4	12/26
Group T	36.0 ± 12.9	70.2 ± 15.0	14/24

Group P = lidocaine-remifentanil-propofol; Group T = lidocaine-remifentanil-thiopental. Values for age and weight are means ± SD. There were no significant differences between groups.

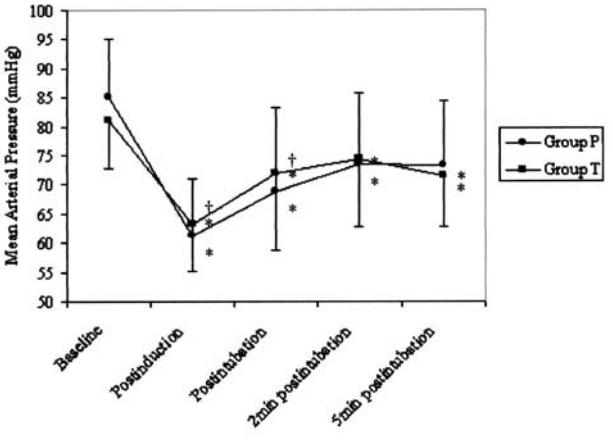

FIGURE 1 Mean arterial pressure in Groups P and T (mean ± SD). *Within groups, statistically significant changes compared with baseline values ($P < 0.05$). †Between groups, statistically significant percentage changes from baseline values ($P < 0.05$). Group P = lidocaine-remifentanil-propofol; Group T = lidocaine-remifentanil-thiopental.

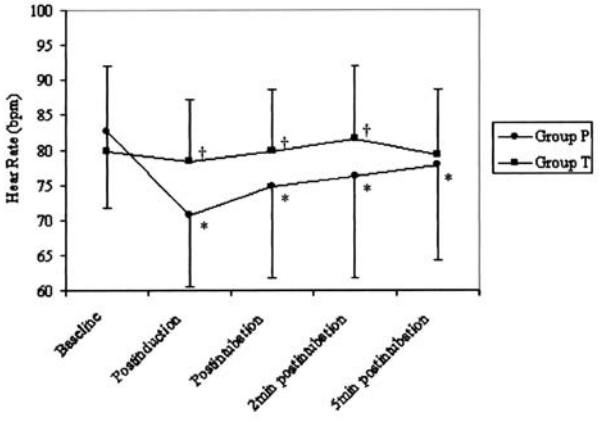

FIGURE 2 Heart rate in Groups P and T (mean ± SD). *Within groups, statistically significant changes compared with baseline values ($P < 0.05$). †Between groups, statistically significant percentage changes from baseline values ($P < 0.05$). Group P = lidocaine-remifentanil-propofol; Group T = lidocaine-remifentanil-thiopental.

intubating scores are shown in Table 1. Intubating conditions were excellent (mask ventilation easy, jaw completely relaxed, vocal cords open, and no movement in response to laryngoscopy and intubation) in 32 (84%) patients in Group P and in 19 (50%) patients in Group T ($P < 0.05$). Good intubating conditions (mask ventilation scored as 1 and the other criteria as 1 or 2) were achieved in 3 (8%) patients in Group P and in 11 (29%) patients in Group T. Poor conditions (one of the criteria scored as 3) were observed in 3 (8%) patients in Group P and in 8 (21%) patients in Group T.

Baseline MAP and HR values were not significantly different between the two groups. However, after induction of anesthesia, MAP decreased significantly in both groups as compared to baseline values and remained lower throughout the investigation ($P < 0.05$). The percentage decrease in MAP values from baseline was significantly higher in Group P than in Group T postinduction (27.4% ± 11.6 *vs* 21.8% ± 10.0) and immediately postintubation (19.0% ± 16.7 *vs* 11.2% ± 14.9); ($P < 0.05$); (Figure 1). In Group P, nine patients developed a decrease of MAP by more than 25% from baseline value for 60 sec with a range from 31 to 48% necessitating the use of ephedrine, while in Group T only one patient required ephedrine ($P < 0.05$). All patients who developed hypotension requiring ephedrine use had excellent intubating conditions.

Following induction of anesthesia, HR decreased in Group P and remained lower than baseline throughout the study ($P < 0.05$); however, HR in Group T did not show significant changes compared to baseline at any time of the investigation. Also, the percentage change from baseline HR values was significantly higher in Group P than in Group T postinduction (13.8% ± 9.7 *vs* 0.5% ± 12.4), immediately postintubation (8.7% ± 13.7 *vs* 2.1% ± 13.1), and two minutes postintubation (7.0% ±14.3 *vs* 3.5% ± 14.3); ($P < 0.05$); (Figure 2). Atropine was not used in any patient.

Discussion

We report a higher incidence of excellent intubating conditions in the lidocaine-remifentanil-propofol group than in the lidocaine-remifentanil-thiopental group. This may be attributed to the fact that propofol is superior to thiopental in decreasing muscle tone and abolishing laryngeal response to tracheal intubation. McKeating *et al.* found that when no muscle relaxants were given, pharyngeal and laryngeal reactivity during laryngoscopy without attempting intubation was more depressed after propofol than after an equipotent dose of thiopental.[10] Also, Barker *et al.* observed, using fibreoptic laryngoscopy, that the vocal cords adducted to a greater extent after induction of anesthesia with thiopental than with propofol.[11] Moreover, Eames *et al.* found that respiratory resistance after tracheal intubation was lower after induction with propofol than after induction with thiopental.[12] Recently, Erhan *et al.* reported that propofol 2 $mg \cdot kg^{-1}$ was superior to thiopental 6 $mg \cdot kg^{-1}$ for tracheal intubation when combined with remifentanil without a muscle relaxant.[7]

In this report, the induction doses of propofol 2 $mg \cdot kg^{-1}$ and thiopental 5 $mg \cdot kg^{-1}$ were judged to be equipotent.[13] However, according to another study, propofol 2.5 $mg \cdot kg^{-1}$ and thiopental 5 $mg \cdot kg^{-1}$ were considered to be equipotent.[14] Had we used the higher dose of propofol, we would have expected the incidence of excellent intubating conditions in Group P to be increased.

In a recent report, the pharmacodynamics of remifentanil and its interaction with propofol were investigated. The authors reported that propofol reduces remifentanil requirements to suppress responses to laryngoscopy, intubation and intra-abdominal surgical stimulation in a synergistic manner.[15] Also, Woods *et al.* suggested that the combination of lidocaine and propofol may have a synergistic effect.[16] Hence, the combination of lidocaine-propofol-remifentanil may have a marked synergistic effect which contributed to the high incidence of excellent intubating conditions.

Addition of lidocaine at induction of anesthesia has been shown to be beneficial in improving intubating conditions.[2,3,16] This may be attributed to a decrease in the incidence and severity of coughing following insertion of the tracheal tube.[2] It is likely that the antitussive effect of lidocaine is caused at least partially by an increase in the depth of general anesthesia;[2] a dose of 1.5 $mg \cdot kg^{-1}$ given three minutes before intubation has been reported to be optimal.[9] In the present report, supplementing remifentanil-thiopental with lidocaine provided excellent conditions in 50% of patients, whereas Durmus *et al.*, in a similar study design, obtained excellent conditions in only 6% of patients when using remifentanil 2 $\mu g \cdot kg^{-1}$ in combination with thiopental 5 $mg \cdot kg^{-1}$ without prior administration of lidocaine.[17] Also, our study shows that adding lidocaine to remifentanil-propofol resulted in excellent intubating conditions in 84% of patients. When Stevens *et al.* used remifentanil 2 $\mu g \cdot kg^{-1}$ in combination with propofol 2 $mg \cdot kg^{-1}$ without prior administration of lidocaine, the number of patients who had excellent intubating conditions did not exceed 50%.[5]

The usual increase in blood pressure and HR following laryngoscopy and tracheal intubation was not observed in the two groups. Similar to previous reports,[18,19] more hypotension and bradycardia followed induction of anesthesia and tracheal intubation in the propofol group than in the thiopental group. The cardiovascular depressant effects of propofol may be attributed to direct myocardial depression and decreased systemic vascular resistance.[20,21] Also, propofol alters the baroreflex mechanism, resulting in a smaller increase in HR for a given decrease in arterial pressure.[22] The decrease in MAP and HR following propofol may be well tolerated in healthy, well hydrated patients, but can be hazardous in elderly patients,[23] and in patients with clinically significant cardiovascular or cerebrovascular disease.

In conclusion, our results show that lidocaine-remifentanil-propofol resulted in excellent intubating conditions in 84% of patients *vs* 50% of patients receiving lidocaine-remifentanil-thiopental. However, more hypotension and bradycardia were observed with propofol than with thiopental; thus, caution is warranted when this technique is used in the elderly or compromised patient.

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