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Comparison of Propofol-remifentanyl with Thiopental-remifentanyl for Tracheal Intubation Without Using Muscle Relaxants, a Double Blind Randomized and Clinical Trial Study

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Abstract: In this study, we compared propofol + remifentanyl with thiopental + remifentanyl without using muscle relaxant for hemodynamic responses and intubation conditions in 100 ASA_I Class I and II patients were randomly assigned to two equal groups. After premedication with midazolam 0.03 mg kg⁻¹ intravenously, remifentanyl 4 µg kg⁻¹ were given in each group. In Group I, propofol 2.5 mg kg⁻¹ and in Group II, thiopental 5 mg kg⁻¹ were given intravenously. After 90s, trachea was intubated. Intubation conditions were classified by the anesthesiologist performing the intubation as: excellent, good, fair and poor. Systolic, mean, diastolic arterial blood pressure and heart rate were recorded as baseline, after the induction and 1, 3, 5, 10, 15 min after the intubation. Data were analyzed by Chi-square, independent t-test, paired t-test and repeated measures ANOVA. $p < 0.05$ was statistically significant. The tracheal intubation conditions were excellent in 60%, good in 32% and fair in 16% of Group I and 42, 42 and 16% in Group II, respectively ($p = 0.166$). The difference in hemodynamic changes in each group and between the two groups were statistically significant ($p = 0.001$). In Group I, 52% and in Group II, 24% need intravenous ephedrine for treatment of hypotension ($p = 0.004$). Atropine were given intravenously in 4 patients of Group I and non of Group II for bradycardia ($p = 0.059$). The results suggest that propofol 2.5 mg kg⁻¹ + remifentanyl 4 µg kg⁻¹ compared with thiopental 5 mg kg⁻¹ + remifentanyl 4 µg kg⁻¹ has no priority for tracheal intubation condition but with more hemodynamic changes.

Key words: Tracheal intubation, remifentanyl, propofol, muscle relaxant

INTRODUCTION

Tracheal intubation is usually facilitated by administration of a muscle relaxant to supplement drugs given for the induction of anesthesia. Neuromuscular blocking drugs and their antagonists have potential side effects that may result in slower recovery. Also in many surgeries, muscle relaxation is undesirable or not required.

Remifentanyl is an ultra short acting opioid, which effectively attenuates the hemodynamic responses to laryngoscopy and tracheal intubation (Glass *et al.*, 1999). The trachea can be reliably intubated without a neuromuscular block in patients who have received remifentanyl followed by propofol (Klemo *et al.*, 2000). Also remifentanyl with thiopental may be useful for tracheal intubation when neuromuscular block is not induced (Mahmut *et al.*, 2003).

In some studies propofol was superior to barbiturates in decreasing muscle tone and abolishing laryngeal response to tracheal intubation (Brown *et al.*, 1991; Hovorka *et al.*, 1991; Steven *et al.*, 1997).

We designed a randomized double-blind clinical trial study to compare the intubation conditions and hemodynamic responses of patients after induction

of anesthesia by propofol 2.5 mg kg⁻¹ + remifentanyl 4 µg kg⁻¹ with thiopental 5 mg kg⁻¹ + remifentanyl 4 µg kg⁻¹ without using muscle relaxants.

MATERIALS AND METHODS

This clinical trial was performed in Dr. Shariati Hospital of Tehran University of Medical Sciences in 2004. After the Institutional Review Board approval and informed consent were given, 100 ASA physical status I and II patients aged 15-60 years, scheduled for elective surgeries under general anesthesia shorter than one hour duration were admitted to the study. The patients were randomized into two equal groups by a computer-generated randomization list that was drawn up by the statistician and the sequence was concealed until interventions were assigned. Exclusion criteria included a history of hypertension, asthma or allergic reactions, drug or alcohol abuse, coronary artery disease and predicted difficulty in intubation or airway maintenance.

After starting standard monitoring of ECG, NIBP and pulse oximeter, all patients were given 5 mL kg⁻¹ normal saline 0.9% and premedicated with midazolam 0.03 mg kg⁻¹ IV, approximately 10 min before the induction

Table 1: Scoring criteria for conditions of intubation

Grade	Scoring Criteria
Excellent	Flaccid relaxation of jaw muscles, good cord visualization, cord well separated-abducted, no bucking
Good	Jaw muscles well relaxed, good cord visualization, slight cord movement, minimal bucking
Fair	Conditions less favorable, jaw muscle relaxed, cord visualization fair but allowing intubation, bucking on intubation
Poor	Poor relaxation of jaw, poor cord visualization, unable to intubate or if intubated marked bucking and body movement

of anesthesia in the operating room. Then remifentanyl (Vial 2 mg, Ultiva™, Glaxowellcome) $4 \mu\text{g kg}^{-1}$ were given over 30 sec. In Group I, propofol (Amp 10 mL propofol-®lipuro1%, B.Brown Melsungen AG) 2.5 mg kg^{-1} and in Group II, thiopental (Vial thiopental 1 g, SANDOZ-Austria) 5 mg kg^{-1} were given intravenously for induction of anesthesia. The coded test syringes of the induction agents were prepared by an independent anesthesiologist in a total volume of 20 mL with envelopes, therefore, all of anesthesia personnel were blinded to the induction agents. Patients were ventilated manually with 100% oxygen, ninety seconds after completion of drug administration, laryngoscopy and tracheal intubation were attempted by one anesthesiologist, using macintosh 3 laryngoscope blade and a 7.5 or 8 mm endotracheal tube for women and men respectively. The anesthesiologist performing the intubation assessed and scored each patient's condition at laryngoscopy and tracheal intubation using criteria in Table 1.

Patients who could not be intubated on the first attempt, were given succinylcholine 1 mg kg^{-1} IV and intubation was completed. Anesthesia was maintained with 0.7% halothane and 50% N_2O . Hypotension (mean arterial blood pressure [MA] <25% from baseline for 60 sec) was treated with ephedrine 5-10 mg IV. bradycardia (heart rate [HR] <50 bpm for 60 sec if hypotension occur) was treated with atropine $20 \mu\text{g kg}^{-1}$ IV. Heart rate (HR), systolic arterial blood pressure (SAP) and diastolic arterial blood pressure (DAP) were recorded as baseline (before any instrumentation), after induction and 1, 3, 5, 10 and 15 min after the intubation.

For sample size calculation we considered excellent and good condition as acceptable and fair and poor as non acceptable condition. Sample size was calculated to detect 20% difference in percentile of acceptable tracheal intubation condition with $\alpha = 0.05$ and statistical power of 0.8. Statistical analysis was performed With SPSS package (SPSS Inc, Chicago, II, USA). Data were analyzed by independent t-test, Chi-square or fisher exact test and repeated measures ANOVA when appropriate. $p < 0.05$ was considered statistically significant.

RESULTS

There were no significant differences in patient's demographic data between the two groups, Table 2 ($p > 0.05$, independent t-test).

Table 2: Comparing demographic data between the two groups

	Group I (n = 50)	Group II (n = 50)
Age (year)	$34.2 \pm 9^*$	$39 \pm 5^*$
Sex (M/F)	18/32	30/20
Weight (kg)	$65.2 \pm 10.4^*$	$64.3 \pm 25.3^*$

*mean \pm SD, There were no significant differences between groups

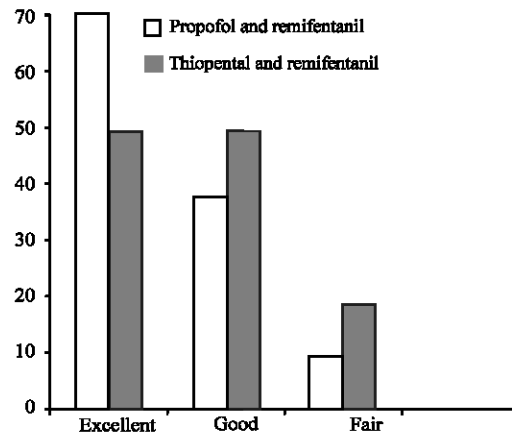


Fig. 1: Distribution of patients in different intubation conditions

The tracheal intubation conditions were considered excellent in 30(60%) patients, good in 16(32%) and fair in 4(16%) patients of Group I and were excellent in 21(42%), good in 21(42%) and fair in 8(16%) patients of Group II respectively ($p = 0.166$, Chi-square). Poor condition did not observe in any group. The percentage of tracheal intubation conditions is shown in Fig. 1.

In Group I, 52% and in Group II, 24% needed intravenous ephedrine for treatment of hypotension (Chi-square, $p = 0.004$). Atropine were given in 4 patients of Group I and none of Group II for bradycardia (fisher exact test, $p = 0.059$).

Hemodynamic changes in MAP and HR were significant in each group and between the two groups (repeated measures ANOVA, $p < 0.05$). In Propofol + remifentanyl group there was more decrease in MAP, Fig. 2 HR did not increase in any group after intubation (Fig. 2).

DISCUSSION

Results of this study suggested that propofol 2.5 mg kg^{-1} + remifentanyl $4 \mu\text{g kg}^{-1}$ compared with thiopental 5 mg kg^{-1} + remifentanyl $4 \mu\text{g kg}^{-1}$ had no statistically difference for tracheal intubation condition in

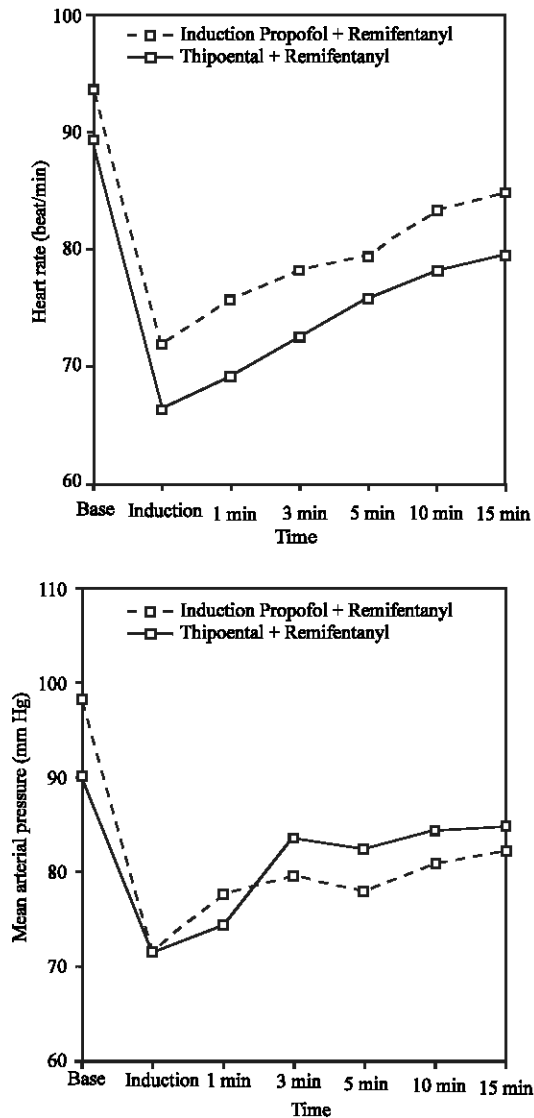


Fig. 2: Heart Rate (HR) and Mean Arterial Pressure (MAP) responses to induction agents and intubation; base = before any instrumentation, induc = after bolus dose of hypnotic agent, 1 min = one minutes after intubation, 3 min = three minutes after intubation, 5 min = 5 min after intubation, 10 min = 10 min after intubation, 15 min = 15 min after intubation

healthy premedicated patients with favorable anatomy. These findings did not correlate with the findings of Brown *et al.* (1991) that observed propofol is superior to barbiturates in decreasing muscle tone and abolishing laryngeal response to tracheal intubation. Propofol + remifentanyl were associated with more decrease in MAP and HR but, HR decrease after the first minute of intubation and then increase compared with thiopental group which supports the findings of Hovorka *et al.* (1991).

Although remifentanyl more than $1 \mu\text{g kg}^{-1}$ is associated with clinically muscle rigidity, no patient manifested signs of rigidity in our study that was correlated with findings of Steven *et al.* (1997). When remifentanyl co-administered with a hypnotic drug, may not cause muscle rigidity (Steven and Wheatly, 1994). Furthermore, pretreatment with benzodiazepines may be effective in preventing opioid induced muscle rigidity (Sunford *et al.*, 1994).

In summary, our results suggested that remifentanyl $4 \mu\text{g kg}^{-1}$ + propofol 2.5 mg kg^{-1} compared with remifentanyl $4 \mu\text{g kg}^{-1}$ + thiopental sodium 5 mg kg^{-1} provide no better condition for tracheal intubation and is associated with more hemodynamic changes in propofol group. So it is recommended for tracheal intubation with opioids and hypnotic agents without using muscle relaxants, to use appropriate induction agent.

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