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Comparing Propofol-ephedrine with Propofol-saline on Intubating Conditions after Priming by Atracurium

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In this study we conducted a double blind, prospective, controlled trial comparing intubating conditions after induction with propofol-ephedrine or propofol-saline, after priming by atracurium. Seventy adult patients received 2 μg kg^{-1} fentanyl and priming dose of atracurium (0.05 mg kg^{-1}) with preoxygeneation. After 2.5 min they were randomly assigned to receive either propofol 2.5 mg kg^{-1} and 140 μg kg^{-1} ephedrine or propofol 2.5 mg kg^{-1} and saline followed by atracurium 0.5 mg kg^{-1}. Tracheal intubation was performed 30 seconds later. Jaw relaxation, vocal cord position and diaphragmatic response were used to assess intubating condition. There was no statistically significant difference in intubating condition between the two groups. Jaw relaxation and response to intubation was better in ephedrine group than saline group ($p = 0.014$ and $p = 0.049$, respectively). Vocal cord positions did not differ significantly between the two groups. There were not statistically significant differences in mean arterial pressure between and within two groups. There was statistically significant difference in heart rate between two groups ($p = 0.01$), but within subject test did not show significant difference in each group. The only complications were 2 cases of self-limiting sinus tachycardia of less than 130 beats min^{-1} in the ephedrine group. In conclusion ephedrine in dose of 140 μg kg^{-1} combining with propofol for intubation after priming by atracurium did not improve intubating condition and induced no clinically acceptable hemodynamic responses.

Key words: Atracurium, ephedrine, intubation, priming, propofol

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INTRODUCTION

The onset time of a neuromuscular blocking drug is an important factor in determining the speed and ease of tracheal intubation. Succinylcholine, a short acting depolarizing muscle relaxant with rapid onset of action (60 sec) has numerous adverse effects, so there has been a continual search for a non depolarizing muscle relaxant (NDMR) that can replicate the onset of succinylcholine (Engbaek and Viby-Mogensen, 1999). Onset time of most of NDMRs are between 3-5 min, so various strategies have been used to shorten their onset time, including increasing the dose and priming (Ortiz-Gomez *et al*., 2005; Schmidt *et al*., 2005). These alternates may provoke a long duration of muscle paralysis or muscle weakness before induction of anesthesia.

Since the onset time of neuromuscular blocking drugs is determined by muscle blood flow and cardiac out put (Donati, 1988; Ezri *et al*., 2003) various studies using induction agents that maintain cardiac out put and blood pressure have been suggested that onset time of muscle relaxants and intubating condition were improved (Leykin *et al*., 2005; Fuchs-Buder *et al*., 1996; Hans *et al*., 1999).

In the study by Tan *et al*. (2002) combination of propofol with ephedrine provided better intubating conditions than propofol alone when followed by rocuronium.

In another study by Albert *et al*. (2000), low dose ephedrine combined with propofol improved intubating condition after cisatracurium.

Since in our country rocuronium a NDMR with faster onset of action is not available and vecuronium, mivacurium and cisatracurium are scarce or very expensive, we used atracurium, the most frequent muscle relaxant available in our operating rooms. We tested the hypothesis that combining propofol with ephedrine as induction agent will improve intubating condition after atracurium administration by priming technique.

MATERIALS AND METHODS

This randomized clinical trial was performed in Dr. Shariati Hospital of Tehran University of Medical Sciences in 2006. After approval from hospital Ethics committee, each patient's informed consent were obtained. Seventy ASA physical status I or II patients aged 18-65 years, who were scheduled for elective surgery under general anesthesia were studied.

Exclusion criteria included the presence of cardiovascular or neuromuscular diseases, any medications known to affect neuromuscular function, anticipated airway difficulties and risk of pulmonary aspiration. On arrival in the operating room, ECG electrodes were applied and oxygen saturation was monitored by pulse oxymeter. An 18-G IV cannula was inserted into a vein of the patient's hand and 5 mL kg^{-1} lactated Ringer's solution was infused. Base line Heart Rate (HR) and non Invasive Blood Pressure (NIBP) were measured and 2 μg kg^{-1} fentanyl (Amp 10 mL , Fentanyl-Janssen™, Belgium) was injected as premedication. Patient were preoxynated by mask and oxygen for 5 min then priming dose of atracurium (Amp 10 mg mL^{-1} Mayne Pharma Plc™, UK) 0.05 mg kg^{-1} was injected intravenously. After 2.5 min, intubating dose of atracurium 0.5 mg kg^{-1} was injected during 30 sec. The patients were randomly assigned to receive 140 μg kg^{-1} ephedrine (Amp 1 mL = 50 mg, Ephedrin Streuli™, Switzerland) in ephedrine group (n = 35) or saline (saline group, n = 35) plus propofol (Amp 20 mL, Propofol 1%. Fresenius™, Germany) 2.5 mg kg^{-1} in equal volume as induction agent just before the intubating dose of atracurium.

During priming interval the patients were also oxygenated and monitored for signs of discomfort, palpebral ptosis, diplopia or respiratory difficulty. Orotracheal intubation was attempted 30 sec after the intubating dose of atracurium and was considered successful only if performed within a 20 sec interval.

Randomization was based on computer-generated codes that were concealed until interactions were assigned. The coded syringes were prepared by an independent anesthetist in equal volume and shape there fore both the anesthesiologist and the patient was blinded to the group assignment.

Tracheal intubation was performed and assessed by an anaesthesiologist with at least 5 years of clinical experience, who was blinded to the group allocation. Intubating conditions were graded according to the criteria of Cooper (Cooper *et al*., 1992), which comprise jaw relaxation, vocal cord position and response to intubation. Jaw relaxation: 0 = poor, 1 = minimal, 2 = moderate and 3 = good; vocal cord position: 0 = closed, 1 = closing, 2 = moving and 3 = open and response to intubation: 0 = severe coughing and bucking, 1 = mild coughing, 2 = light diaphragmatic movement and 3 = none. A score of 8 and 9 was considered excellent, 6-7 good, 3-5 poor and 0-2 bad.

Excellent and good conditions were considered clinically acceptable while fair or poor conditions were considered unacceptable. The primary outcome was the number of patients with clinically acceptable intubating conditions.

Non Invasive Blood Pressure (NIBP) and heart rate were recorded as base line (before premedication), 1 min after propofol injection and 1 min after tracheal intubation. The presence of arrhythmias on the ECG monitor and other complications during priming interval were also recorded.

Statistical analysis: For sample size calculation we considered excellent and good condition as acceptable and poor and bad as non acceptable condition. Sample size was calculated to detect 25% 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 version 11.5. Normality of distribution was tested by Kolmogorov-Smirnov test. Data were analyzed by independed sample t-test, repeated measures ANOVA, chi-square or fisher exact test when appropriate. $p<0.05$ was considered statistically significant.

RESULTS

There were no significant differences in demographic data between the two groups, (Table 1) (Independent sample t-test, Chi square). All intubations were successful and performed within a 20 sec interval and there were no statistically significant differences in intubating conditions between the two groups (Table 2) (chi-square). Jaw relaxation and response to intubation was better in ephedrine group ($p = 0.014$ and $p = 0.049$, respectively) but vocal cord positions did not differ significantly between the two groups (Table 3). The baseline values of MAP and HR did not differ between the two groups (independent sample t-test). There were not statistically significant differences in MAP between and within two groups (repeated measures ANOVA). Differences in HR was statistically significant between the two groups (repeated measures ANOVA, between subject effects, $p = 0.01$), but within subject test did not show significant difference in each group. The only complications were 2 cases of self-limiting sinus tachycardia of less than 130 beats min^{-1} in the ephedrine group.

Table 1: Comparing demographic data between the study groups

Variables	Ephedrine group (n = 35)	Saline group (n = 35)
Age (year)*	37±15	34±12
Weight (kg)*	66±12	67±11
Sex (M/F)	14/21	18/17
ASA class (I/II)	23/12	20/15

*Data are presented as mean±SD

Table 2: Comparing intubating conditions between the study groups

Intubating condition	Ephedrine group (n = 35)	Saline group (n = 35)
Excellent	22 (63)*	14 (40)
Good	9 (26)	17 (49)
Poor	4 (11)	4 (11)

*Data are presented as number (percent) of patients

Table 3: Comparing jaw relaxation, vocal cord position and response to intubation between the study groups

Criteria for intubating condition	Ephedrine group	Saline group	p-value
Jaw relaxation			p = 0.014
Minimal	1 (2.9*)	3 (8.6)	
Moderate	7 (20)	17 (48.6)	
Good	27 (77.1)	15 (42.9)	
Vocal cord position			NS**
Closed	1 (2.9)	0	
Closing	2 (5.7)	6 (17.1)	
Moving	6 (17.1)	7 (20)	
Open	26 (74.3)	22 (6.29)	
Response to intubation			p = 0.049
Sever cough	1 (2.9)	0	
Mild cough	4 (11.4)	3 (8.6)	
Mild diaphragm move	9 (25.7)	20 (57.1)	
None	21 (60)	12 (34.3)	

**NS: Non Significant, *Data are presented as number (%) of patients

DISCUSSION

In this study we compared propofol-ephedrine with propofol-saline on intubating condition after priming with atracurium. We used ephedrine because it is a weak sympathomometic agent which produces venoconstriction more than arterial constriction, improving venous return, increasing cardiac out put and thus muscle blood flow. The circulating time to the target organ and its blood flow partly determine the onset time of the neuromuscular block that can improve intubating condition (Lawson and Meyer, 2001).

The main finding of this study is that combination of propofol-ephedrine compared with propofol-saline did not improve intubating condition after priming by atracurium. This finding is not correlated with the study by Tan *et al.* (2000) which comparing propofol-ephedrine with propofol alone on intubating condition after rocuronium. They resulted that intubating condition was better in ephedrine group.

In the study by Albert *et al.* (2000) propofol-ephedrine compared with propofol-saline on intubating condition after cisatracurium and intubating condition was better in ephedrine group.

In present, Jaw relaxation and response to intubation was better in ephedrine group but Vocal cord positions did not differ significantly between the two groups. In Tan *et al.* (2002) study Vocal cord position and response to intubation were significantly better in the propofol-ephedrine group, although jaw relaxation was similar.

The differences in present study with Tan *et al.* (2002) and Albert *et al.* (2000) studies may be due to our different type of muscle relaxant and using premedication that may help for better intubating condition in both groups but other factors should be included.

We had no statistically significant differences in MAP between and within two groups. HR was statistically but not clinically (more than 30% of normal) higher in ephedrine group. Within subject test did not show significant difference in HR of each group. In Tan *et al.* (2002) study MAP and HR were significantly increased in the propofol-ephedrine group that was not correlated with present study.

These differences may be due to using premedication in present study, however histamine release of atracurium may be partially responsible.

Further study may be needed to evaluate the effects of different doses of ephedrine on intubating condition after priming by atracurium or other NDMRs.

In conclusion ephedrine in dose of 140 μg kg^{-1} combining with propofol for intubation after priming by atracurium did not improve intubating condition and induced no clinically acceptable hemodynamic responses.

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