Research Article

A study to evaluate effect of ephedrine on intubating conditions and haemodynamic parameters using low dose rocuronium with different induction agents

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ABSTRACT

Background: There has been a search for an ideal muscle relaxant which might provide ideal intubating conditions in ultra short duration with minimal side effects.

Objective: To compare the intubating conditions and haemodynamic response one minute after rocuronium (0.6 mg/kg) administration, using three different induction techniques i.e. thiopentone, propofol and propofol with ephedrine.

Materials and Methods: Seventy five adult patients were randomized into one of three groups: groups-A and B received thiopentone and propofol respectively and group -C received propofol with ephedrine. All groups received rocuronium 0.6mg/kg following administration of their respective drugs. Tracheal intubation was performed one minute later. An experienced anaesthesiologist assessed the intubating conditions. Haemodynamic parameters were recorded before induction of anaesthesia, post induction and one and three minutes after intubation.

Results: Patient's characteristics and baseline haemodynamic parameters were comparable in all three groups. Intubating conditions were significantly better in propofol-ephedrine group as compared to other two groups. Following intubation, rise in heart rate and blood pressure was more marked in propofol-ephedrine group as compared to other groups.

Conclusion: Rocuronium 0.6 mg/kg provides better intubating conditions at one minute with propofol-ephedrine combination as compared to propofol alone or thiopentone.

Key words: propofol, thiopentone, ephedrine, rocuronium, intubating conditions, hemodynamic

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INTRODUCTION

Ever since the advent of anaesthesia, anaesthesiologists have been in search of an ideal muscle relaxant which might provide ideal intubating conditions in ultra short duration with minimal side effects. Succinylcholine has been the drug of choice since its introduction in 1952. Doses of 1-1.5 mg/kg provide excellent intubating conditions in 60-90 seconds and duration of action is also very short.[1] Unfortunately succinylcholine has many side effects and contraindications.[2] Rocuronium has emerged as the preferred non-depolarizing neuromuscular blocking agent for rapid intubation. It provides good intubating conditions in 60-90 seconds in doses of 0.9-1.2 mg/kg,[3-7] but large doses of rocuronium result in prolonged duration of action,[8] making it unsuitable for short operations. Increasing the dosage of rocuronium from 0.6 mg/kg (twice the ED_{95}) to 1.2 mg/kg (four times the ED_{95}) shortened the onset time of complete neuromuscular blockade from 89 ± 33 seconds (mean ± SD) to 55 ± 14 seconds but significantly prolonged the clinical duration from 37 ± 15 minutes to 73 ± 32 minutes.[7]

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Induction agents that maintain cardiac output and blood pressure, e.g. ketamine[8] and etomidate,[9] have provided faster onset time and better intubating conditions with rocuronium. Addition of ephedrine to different induction agents has also been shown to shorten onset time of different muscle relaxants.[10-13] In this study, we compared the intubating conditions and haemodynamic response one minute after rocuronium (0.6 mg/kg) administration, using three different induction techniques i.e. thiopentone, propofol and propofol with ephedrine.

MATERIALS AND METHODS

Inclusion and exclusion criteria

This prospective randomized study was conducted after obtaining approval from institutional ethics committee of Pt. B. D. Sharma PGIMS Rohtak, India. After obtaining written informed consent, seventy five patients of American Society of Anesthesiologists (ASA) Grade I and II, of both sexes, scheduled for elective surgery, requiring general anaesthesia and endotracheal intubation were included in the study. Patients with difficult intubation, low pulmonary compliance, obese patients and those with history of ischemic heart disease or hypertension were excluded from the study.

Study design

All the patients were randomly assigned to one of the following three groups. Group A (n=25) patients were induced with injection thiopentone 5 mg/kg i.v. given over 15 seconds.[8] Group B (n=25) patients were induced with injection propofol 2.5 mg/kg iv given over 15 seconds.[14] Group C (n=25) patients were induced with injection propofol 2.5 mg/kg iv with ephedrine (15 mg added to 20 ml) given over 15 seconds.[14]

Study procedure

All patients were kept fasting for six hours. Tab alprazolam 0.25 mg orally at bedtime and two hours prior to surgery with a sip of water was given as premedication.

On arrival in the operating room, intravenous line was secured and standard monitoring (ECG, SPO_2, and automated blood pressure) was instituted. Patients were oxygenated for three minutes. Induction agent was then administered as per the study protocol. Injection rocuronium 0.6 mg/kg was administered to facilitate endotracheal intubation. All patients were manually ventilated using O_2 (33%), N_2O (67%) and sevoflurane (1%) with Bains circuit. At the end of one minute after rocuronium administration, endotracheal intubation was done in all the three groups using 7 mm ID and 8 mm ID cuffed endotracheal tubes in female and male patients respectively. The intubating conditions were graded using criteria of Copper et al.[3] Jaw relaxation : 0 = poor, 1= minimal, 2 = moderate, 3 = good; Vocal cord position: 0 = closed, 1 = closing, 2 = moving, 3 = open; Response to intubation: 0 = severe coughing or bucking, 1= mild coughing, 2 = light diaphragmatic movement and 3 = none. A score of 8-9 was considered excellent, 6-7 good, 3-5 poor and 0-2 bad. Excellent and good conditions were considered clinically acceptable, while poor or bad conditions were considered clinically unacceptable. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP) and heart rate were recorded at following times: Baseline (T_0), Just before intubation (T_B), One and three minutes after intubation (T_1, T_3). Further anaesthesia was maintained with oxygen (33%), nitrous oxide (67%) and halothane (0.5%). Inj. fentanyl was given for analgesia. At the end of surgery, all patients were reversed with inj. glycopyrolate and inj. neostigmine.

Statistical analysis

Data was analyzed statistically using one way ANOVA test, chi square test, paired and unpaired t test using software SPSS version 10.

RESULTS

Demographic data were comparable in all the three groups (Table 1). Parameters of intubating conditions like jaw relaxation, response to intubation and vocal cord position were comparable in all the three groups. However, 5 patients in group A and 3 in group B were with poor intubation score (unacceptable intubating condition) as compared to group C, in which all patients had acceptable intubating condition. Statistically there were more patients with excellent intubation score in propofol-ephedrine group (group - C) as compared to group A and B (Table 2). Baseline heart rate was comparable in three groups but significant variation in heart rate were seen after induction of anesthesia. (Table 3). Mean blood pressure (Table 4) before intubation (TB) showed no significant difference from baseline values (T0) in groups A and C, but decreased significantly in group B (91.1, 7.17 (average, S.D.) to 74.3, 6.8). Mean blood pressure was significantly higher than baseline at all times following intubation in groups A and C. There were significant differences in the average mean blood pressures between group B and groups A and C at all times following induction (Table 4).

Table 1 : Mean age and weight of subjects

Group (treatment)	Weight in kg (Mean ± SD)	Age in years (Mean ± SD)
A (Thiopentone)	57.88 ± 8.26	32.08 ± .62
B (Propofol)	57.80 ± 8.64	33.80 ± 8.33
C (Propofol + ephedrine)	57.44 ± 7.93	32.96 ± 8.03

Table 2: Distribution of total intubation score

Group	Total intubation score			
	Bad	Poor	Good	Excellent
A (Thiopentone)	Nil	5	17	3
B (Propofol)	Nil	3	18	4
C (Propofol + ephedrine)	Nil	Nil	12	13

P values for group with chi sq values: A, B, C combined is 0.004 (chi sq = 15.16). A & B is 0.715 (chi sq = 0.671). B & C is 0.011 (chi sq = 8.96). A & C is 0.002 (chi sq = 12.12)

Table 3: Comparison of variation in heart rate among subjects at different time

Groups	Baseline	Just before Intubation	One min after intubation	3 min after intubation
Group A, vs. B (p value)	83.72 ± 7.24 83.48 ± 9.63 (0.92)	94.92 ± 10.07 94.72 ± 7.70 (0.93)	106.04 ± 9.30 105.00 ± 7.59 (0.66)	103.36 ± 8.47 101.00 ± 7.49 (0.30)
Group B vs. C (p value)	83.48 ± 9.63 80.16 ± 9.04 (0.21)	94.72 ± 7.70 86.36 ± 8.18 (0.00)*	105.00 ± 7.59 110.76 ± 7.45 (0.01)*	101.00 ± 7.49 105.52 ± 7.27 (0.03)*
Group A vs. C (p value)	83.72 ± 7.24 80.16 ± 9.04 (0.13)	94.92 ± 10.07 86.36 ± 8.18 (0.00)*	106.04 ± 9.30 110.76 ± 7.45 (0.05)*	103.36 ± 8.47 105.52 ± 7.27 (0.33)

* p ≤ 0.05

Table 4: Comparison of mean blood pressure among three groups at different time interval

Groups	Baseline	Just before Intubation	One min after intubation	3 min after intubation
Group A vs B (p value)	96.00 ± 11.76 91.08 ± 7.17 (0.08)	87.56 ± 8.81 74.28 ± 6.80 (0.00)*	109.48 ± 11.36 100.04 ± 9.84 (0.00)*	102.88 ± 7.65 94.84 ±1 0.23(0.00)*
Group B vs C (p value)	91.08 ± 7.17 92.20 ± 7.77 (0.59)	74.28 ± 6.80 87.68 ± 8.29 (0.00)*	100.04 ± 9.84 114.76 ± 10.63 (0.00)*	94.84 ± 10.23 106.76 ± 10.38 (0.00)*
Group A vs C (p value)	96.00 ± 11.76	87.56 ± 8.81	109.48 ± 11.36	102.88 ± 7.65

* p ≤ 0.05

DISCUSSION

Onset time of a neuromuscular blocking agent partially depends upon the speed with which the drug reaches neuromuscular junction, which, in turn depend on cardiac output and muscle blood flow. Studies using induction agent like ketamine and etomidate, which maintain cardiac output and blood pressure have found that use of these drugs was associated with faster onset of action and better intubating conditions with rocuronium.[8,9]

Propofol and thiopentone are commonly used induction agents. These agents cause fall in blood pressure when used for induction of anaesthesia. It was postulated that this fall in blood pressure associated with thiopentone and propofol results in delayed reach of muscle relaxant at laryngeal muscles, which is responsible for delayed onset.[8] Ephedrine is well known to counter fall in blood pressure during spinal anaesthesia.[15] Ephedrine when added to propofol, counters fall in blood pressure and provides better hemodynamic profile. Gamlin et al observed that addition of 15-20 mg ephedrine to 1% (20 ml) propofol was very effective in maintaining blood pressure at pre-induction value but ephedrine in a dose of 10 mg was ineffective.[16] In various studies, addition of ephedrine to propofol has shortened the onset time of action of muscle relaxants like succinylcholine,[10] cisatracurium[11] and vecuronium.[17]

We hypothesized that the addition of ephedrine to propofol induction will produce better intubation conditions than propofol alone based upon the theoretical assumption that increased cardiac output due to the ephedrine will produce a faster onset time of rocuronium. In our study, propofol-ephedrine combination provided better intubating conditions than thiopentone and propofol alone. The better intubating conditions in propofol-ephedrine group were proposed to be due to the effect of ephedrine, resulting in an increased cardiac output and tissue perfusion and therefore a faster delivery of rocuronium to the laryngeal and diaphragmatic muscles.[13] We also found that propofol alone provided better intubating conditions than thiopentone in spite of causing more fall in blood pressure. This was thought to be due to property of propofol to depress laryngeal and pharyngeal reflexes.[18]

We also observed that after induction blood pressure decreased in all three groups. This decrease was more marked in propofol group compared to propofol-ephedrine group. Following intubation there was significant rise in blood pressure. This rise was more marked in propofol-ephedrine group and less in propofol group and persisted till the end of study period. This rise might be detrimental in patients with ischemic heart disease, increased intracranial tension and increased intraocular pressure.

Our study has some limitations. We did not measure cardiac output which could have confirmed and quantitatively measured effect of ephedrine on cardiac output. The effects of ephedrine on muscular blood flow have not been measured so far in the clinical setting. Hence, differences in regional blood flow promoted by ephedrine may only be speculated. We used only single dose of ephedrine (15 mg) which caused significant haemodynamic changes. There is a need to find optimum dose of ephedrine which shortens the onset time without causing potentially harmful haemodynamic changes. Studies using different doses of ephedrine may be helpful in finding optimum dose of ephedrine.

In conclusion, rocuronium 0.6 mg/kg provides better intubating conditions at one minute with propofol-ephedrine combination as compared to propofol alone and thiopentone.

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