Original Article

Effect of ephedrine on rapid intubation and haemodynamics using propofol and rocuronium: A randomized controlled trial

SM Abdul Alim[1*], Md. Mozaffer Hossain[2], UH Shahera Khatun[3]

[1]Assistant Registrar, Central Police Hospital, Dhaka, [2]Consultant, Department of Anaesthesiology and ICU, DMCH, Dhaka, [3]Professor and Head, Department of Anaesthesiology and ICU, DMCH, Dhaka

**** Corresponding author:*** *Assistant Registrar, Central Police Hospital, Dhaka*

Abstract:

Ephedrine is a suitable drug to increase the cardiac output and tissue perfusion, in adequate dose, resulting in faster delivery of drug to muscles. This study was designed to compare the effect of pretreatment with ephedrine 75,100, 150 µg/kg and saline on intubating conditions and haemodynamics during rapid tracheal intubation using propofol and rocuronium. The aim of this study was to evaluate the effects of different doses of ephedrine, given before induction, on intubating conditions and haemodynamics during rapid tracheal intubation. One hundred and twenty adult patients randomized into one of the four groups- I, II, III and IV were received iv ephedrine 75, 100, 150µg/kg and saline 0.9% (5ml) respectively, one minutes before administering propofol 2.5 mg/kg and rocuronium 0.6 mg/kg. Patients' mean arterial pressure, heart rate, were recorded before induction (base line), just before intubation, and 1, 3, and 5 minutes after tracheal intubation. Data were analysed between the groups and within the groups using ANOVA test and X^2-test. A p*-value of <0.05 were considered as significant. Patients characteristics, baseline heart rate, and mean arterial pressure were comparable between the groups. Iutubating conditions were significantly better in group II (p=0.002). Pulse rate at different times were statistically significant (p<0.001) except base line and just before intubation. The mean difference of average mean blood pressure at different times were statistically significant (p<0.05) except baseline. In conclusion, pre-treatment with ephedrine 100 µgm/kg improved the intubating conditions during rapid tracheal intubation using propofol and rocuronium.*

Keywords*: propofol, haemodynamics, intubation condition, premedication, ephedrine.*

(Journal of BSA, 2009; 22(1): 16-20)

Introduction:

Laryngoscopy and endotracheal intubation is performed during most of the general anaesthetic procedure. The time from loss of consciousness to tracheal intubatoion is a period during which the patient is at risk of hypoxia and pulmonary aspiration. To minimize the chance of hypoxia, regurgitation and aspiration of gastric content the rapid sequence intubation is commonly used to secure the patients airway[1]. Traditionally, suxamethonium is the gold standard and drug of choice for rapid sequence intubation but some side effects preclude its use in all patients[2]. Rocuronium is the currently preferred non-depolarizing neuromuscular blocking agent used as an alternative to suxamethonium for rapid tracheal intubation. The onset time of a neuromuscular blocking drug is an important factor in determining the speed and ease with which the trachea can be intubated during a rapid sequence intubation[3]. In rapid sequence intubation, the time from loss of consciousness to tracheal intubation is usually determined by the establishment of neuromuscular blockade, so it is usually desirable to use a muscle relaxant with a short onset time. The onset time is partly determined by the speed with which these drugs reach the neuromuscular junction, a factor that appears to be proportional to cardiac output and muscle blood flow[4]. Rocuronium used in the lower dose of 0.6 mg/kg for rapid tracheal intubation is

known to provide suboptimal intubation conditions in 20-25% patients [5,6]. This could be as a result of a decrease in cardiac output cause by the induction agent, resulting in slower onset of action at the laryngeal muscles and the diaphragm [7,8]. So it is desirable to use a suitable drug just before induction to increase the cardiac output and tissue perfusion, and resulting in faster delivery of rocuronium to laryngeal and diaphragmatic muscles, for rapid onset of action of rocuronium and improving the intubation conditions during rapid sequence induction. Objective of present study is to compare the effect of pre-treatment with ephedrine 75, 100, 150 μg/kg and saline on intubating conditions and haemodynamics during rapid tracheal intubation using propofol and rocuronium.

Materials and Methods:

This study was conducted after obtaining approval from the institutional ethical committee. ASA physical status I or II patents, either male or female, between 18-60 years of age undergoing elective surgical procedures requiring general tracheal anaesthesia were included. Patients with concomitant medical illness, anticipated difficult airway, pregnancy, presence of drugs that influence induction and history of known allergy to drugs were excluded from the study. Patients were randomly selected into one of the four groups by sealed envelope lottery technique. Sample size was 30 in each group. The four groups were- Group I, Group II, Group III and Group VI (control).

Selection of patients, grouping, entry of name of the patient in the case record form and the written informed consent was taken from all patients on the pre-operative day. Pre-medication with oral diazepam .1 mg/kg was given in the night before the surgery. Patients were fasted 6 hours before operation.

After transferring the patents into the operating room, standard monitoring (five lead ECG, SpO_2, NIBP) was instituted. I/V lactated Ringer's solution was started at a rate of 2 ml/kg/h. Fentanyl 1 μgm/kg was given 1 min after the start of oxygenation. Then one minute after ephedrine in the dosage of 75, 100, or 150μgm/kg in the groups I, II, III respectively, or saline 0.9% (5ml) for group IV was injected. Three minutes after pre-oxygenation with 100% oxygen anesthesia was induced with propofol 2.5 mg/kg. Mask ventilation was not done till tracheal intubation, unless the oxygen saturation goes to <95%.

Laryngoscopy and tracheal intubation was done by investigator with an appropriate sized Macintosh blade 60 s after administration of rocuronium. The intubating conditions were assessed as per the intubation scoring system of the Consensus Conference on Good Clinical Research Practice in Pharmacodynamic Studies of Neuromuscular Blocking Agents, Copenhagen consensus[15]. Oral tracheal tubes 7.0 and 8.0 mm internal diameter were used for female and male respectively. The cuff was inflated with air until the disappearance of a leak on positive pressure ventilation.

Patients' mean arterial pressure, heart rate, and oxygen saturation were recorded before induction (base line), just before intubation, and 1, 3, and 5 minutes after tracheal intubation. TOF ratio, and response of the patient to tracheal intubation were recorded (Table II). Anaesthesia was maintained with oxygen 40%, nitrous oxide 60% and halothane with intermetant positive pressure ventilation maintaining normocapnia. All relevant data were collected from each patient by a pre-designed questionnaire and comparison was made between the groups. Data were analyzed using SPSS version 12 for Windows. ANOVA test and X^2-test were used for comparative analyses. A p-value of <0.05 was considered as significant.

Results:

Demographic characteristics were comparable among the groups (Table I). Baseline heart rate and mean arterial pressures were comparable between the groups.

The mean difference of pulse rate (Fig-1) at different times were statistically significant ($p<0.001$) except base line and just before intubation. The mean difference of average mean blood pressure (Fig-2) at different times were statistically significant ($p<0.05$) except baseline. The mean difference of TOF ratio at 60 seconds was statistically significant ($p<0.001$). The intubation condition (Table III) was statistically significant ($p<0.002$) in group II when compared with group IV.

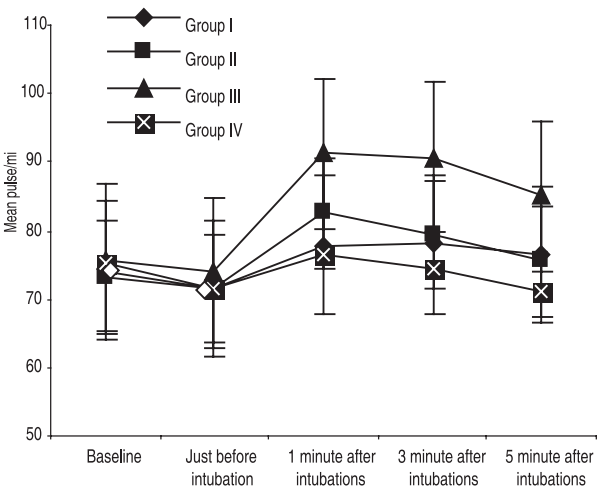

Fig.-1: *Line diagram showing mean pulse at different times in four groups*

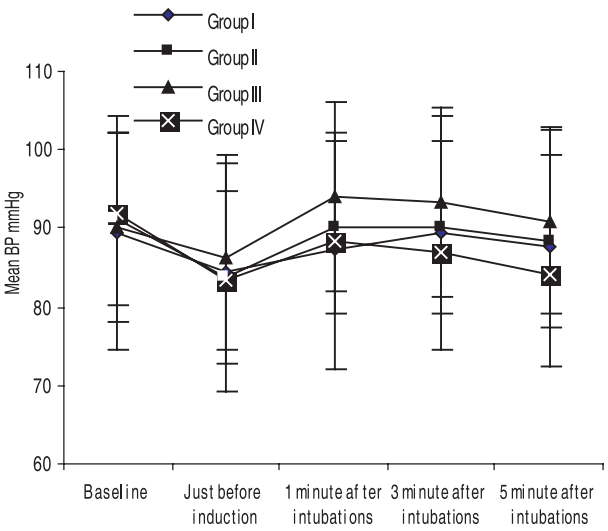

Fig-2: *Line diagram showing mean blood pressure at different times in four groups*

Table-I

Demographic characteristics of the study subjects (N=120).

Demographic variables	Group I(n=30)		Group II(n=30)		Group III(n=30)		Group IV(n=30)	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Age (years)	35.6	±10.6	32.9	±9.1	36.6	±10.9	31.5	±9.5
Weight (kg)	54.3	±6.1	54.7	±6.1	54.7	±5.0	55.9	±5.6
Male	9	(30.0)	9	(30.0)	12	(40.0)	9	(30.0)
Female	21	(70.0)	21	(70.0)	18	(60.0)	21	(70.0)

Values within parenthesis are expressed as percentage over column total,

Chi square =1.03, df=3, p=0.795

Not significant (p > 0.05) with chi square test for sex distribution,

Table-II

Scoring and Assessment of intubating conditions.

Score	Jaw relaxation (easy to laryngoscopy)	Vocal cords	Response to intubation
0	Poor (impossible)	Closed	Severe Coughing or bucking
1	Minimal (difficult)	Closing	Mild coughing
2	Moderate (fair)	Moving	Slight diaphramatic movement
3	Good (easy)	Open	None

Excellent (score8-9), Good (score 6-7), Fair (score 3-5), Poor (score 0-2)

Table-III

Assessment of intubation condition of the patients between groups

Pair group	Excellent		Good		Fair/poor		Chi value	P value
	n	%	n	%	n	%		
Group I	15	50.0	10	33.3	5	16.6	4.72	0.094^{NS}
Group IV	7	23.3	14	46.7	9	30.0		
Group II	20	66.7	8	26.7	2	6.7	12.35	<0.002
Group IV	7	23.3	14	46.7	9	30.0		
Group III	12	40.0	10	33.3	8	26.7	2.04	0.360^{NS}
Group IV	7	23.3	14	46.7	9	30.0		

Chi square =13.40, df=6, p=0.037
Significant ($p < 0.05$) with chi square test

Discussion:

The results from the present study show that ephedrine in the dose of 100μgm/kg given intravenously before rapid tracheal intubation with propofol 2.5mg/kg and rocuronium 0.6 mg/kg improved intubation conditions. However, there was no clinically significant difference in mean arterial pressure and heart rate among the groups during the first 5 minutes after intubation. In this study age ranged of the patients in four groups were belongs to 19 to 55 years. Male female ratio was comparable with the earlier studies[9-12]. The mean heart rate was comparatively higher in group III followed by group II, group I and than group IV, since 1 minute to 5 minutes after intubations, however group I was almost stable. The heart rate difference were found statistically significant ($p<0.001$) from 1 minute to 5 minutes after intubations. The result obtained in the present study is comparable with the previous studies [3,9,13,14]. The mean arterial pressure at different times was found 89.4±4.6mmHg in group I, 91.1±4.1mmHg in group II, 90.2±3.7mmHg in group III and 91.9±3.8mmHg in group IV during baseline. But Just before intubation the mean(±SD) mean arterial pressure (MAP) was significantly ($p<0.05$) decline in all four groups. However one minute after intubation the mean arterial pressure was significantly raised in all four groups.Three minute and 5 minutes after intubation the mean arterial pressure were almost comparable in group I and group II but discrepancy were observed in group III and group IV. Mean arterial pressure at different times were statistically significant. Despite ephedrine pre-treatment, there was a decrease in mean arterial pressure in the immediate post-induction period. There was no clinically significant difference in mean arterial pressure and heart rate among the groups during the first 5 min after intubation (considering 20% change as clinically significant). Thus, prophylactic injection of ephedrine only attenuates, but does not completely abolish the decrease in arterial pressure associated with induction of anaesthesia using fentanyl and propofol. The present study findings strengthen by the finding of the earlier authors[14] . TOF ratio at the end of 60 s of rocuronium injection were comparable among the groups. In the present study the mean TOF ratio at 60 sec was 62.7±4.4 in group I, 57.2±5.2 in group II, 66.5±5.3 in group III and 72.8±5.3 in group IV just before intubation and the mean difference of TOF ratio was statistically significant ($p<0.05$) in all four groups, which support the previous observation [14].

Assessment of intubation condition of the patients was observed in the current study and the difference was statistically significant ($p<0.05$), which indicates that the excellent assessment was significantly higher in group II than others groups. In this study it was observed that the ephedrine 75 and 100 μmg/kg pretreatment before propofol induction resulted in better intubating conditions, similar to the findings of the earlier study. An additional finding is that increasing the dosage of ephedrine from 100 to 150 μmg/ kg did not improve the intubating conditions. Probably, ephedrine in the excess dosages may produce vasoconstriction of blood vessels supplying laryngeal muscles, thus limiting the access of the relaxant to its site of action.

The present study strongly support the earlier study[14].

Conclusion:

Pre-treatment with ephedrine 100 µgm/kg improves the intubating conditions during rapid tracheal intubation and reduce degree of hypotension using propofol and rocuronium.

References:

1. McCourt, Salmela L, Mirakhur RK, *et al*. Comparison of rocuronium and succinylcholine for use during rapid sequence induction of anaesthesia. Anaesthesia 1998;**53**: 867-71.
2. Lee C. Succinylcholine update. Curr Opin Anaesthesiol 1993;**6**: 709-14.
3. Tan CH, Onisong MK, Chiu WKY. The Influence of induction technique on intubating conditions 1 minute after rocuronium administration: comparison of propofol-ephedrine combination and propofol. Anaesthesia 2002;**57**:223-6.
4. HernanR. Munoz, MD, MSc, Alejandro G. *et al*. Gonzalez, MD, and Arnaldo E. Perez, MD The Effect of Ephedrine on the Onset Time of Rocuronium. Anesth Analg. 1997; **85**: 437-40.
5. Sparr HJ, Giesinger H, Ulmer M, *et al*. Influence of induction technique on intubating conditions after rocuronium in adults: comparison with rapid sequence induction using thiopentone and suxamethonium. Br J Anaesth 1996;**77**: 339-42.
6. Sparr HJ, Luger TJ, Heidegger T, *et al*. Comparison of intubating conditions after rocuronium and suxamethonium following 'rapid- sequence inducton' with thiopentone in elective cases. Acta Anaesthesiol Scand 1996; **40**: 425-30.
7. Baraka AS, Sayyid SS, Assaf BA. Thiopental-rocuronium versus ketamine-rocuronium for rapid-sequence induction in parturients undergoing caesarean section. Anesth Analg 1997;**84**: 1104-7.
8. Fuchs-Buder T, Sparr HJ, Zweigenfu T. Thiopental or etomidate for rapid sequence induction with rocuronium. Br J Anaesth 1998;**80**: 504-6.
9. Munoz HR, Gonzales AG, Perez AE. The effect of ephedrine on the onset time of rocuronium. Anesth Analg 1997;**85**:437-40.
10. Puhringer FK, Khuenl-Brady KS, Koller J, *et al*. Evaluation of the endotracheal intubating conditions of rocuronium (Org 9426) and succinylcholine in outpatient surgery. Anesth and Analg 1992; **75**: 37-40.
11. Puhringer FK, Khuenl-Brady KS, Mitterschiffthaler G. Rocuronium bromide: time course of action in underweight, normal weight,overweight, and obese patients. Eur J Anaesthesiol 1995; 12(Suppl. 11); 107-10.
12. Ezri T, Szmuk P, Waters RD, *et al*.Changes in onset time of rocuronium in patient pretreated with ephedrine and esmolol- the role of cardiac output. Acta Anaesthesiol Scand 2003;**47**. 1067-72.
13. Gamlin F, Freeman J, Winslow L, *et al*. The haemodynamic effect of propofol in combination with ephedrine in elderly patients (ASA group 3 and 4). Anaesth Intensive Care1999;**27**: 477-8.
14. Gamlin F, Vucevic M, Winslow L, *et al*. The haemodynamic effect of propofol in combination with ephedrine. Anaesthesia1996;**51**: 488-91.
15. Viby-Mogensen J, Engback J, Eriksson LI *et al*. Good clinical research practice (GCRP) in pharmacodynamic studies of neuromuscular blocking agents. Acta Anaesthesiol Scand 1996;**40**: 59-74.