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Original Research Article

A Study to Assess the Effects of Ephedrine Pre-Treatment on Intubating Conditions Along with Propofol and Rocuronium.

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Introduction: Ephedrine reduces the hypotension following propofol administration. The present study was done to compare the influence of pre treatment with a low dose of intravenous ephedrine on the intubating conditions and its effects on haemodynamics during rapid tracheal intubation using propofol, rocuronium bromide.

Methods: It was conducted Rangaraya Medical College. Adults on elective surgery require general anaesthesia were includede. Pregnant women, known hypersensitivity to the study drugs, anticipated difficult airway, Mallampati grade III, IV were excluded. Premedicated at bed time of the previous night of surgery, nil orally 10 pm onwards. Randomly divided into group Ephedrine Rocuronium (ER) received ephedrine 70 µg/kg diluted to 5 ml with normal saline and normal saline rocuronium (NR) group received 5 ml normal saline at the time of preoxygenation. One minute later, induced with intravenous Propofol 2.5 mg/kg with preservative free lidocaine 2%, 1ml for every 10 ml of propofol, injected over 30 seconds. One minute later, intravenous rocuronium was given and mask oxygenation was continued, laryngoscopye was performed 60 sec later. Heart rate (HR), blood pressuere (BP) were recorded. Care was taken to avoid any stimulus during the study period. $P < 0.05$ was considered to be statically signifcant.

Results: Total 120 members were included, 60 each group. Intubating conditions were statically significant. Statistically there was no significant difference for mean duration of laryngoscopy, base line HR. The baseline systolic, diagnostic BP and mean arterial pressure were comparable.

Conclusion: Ephedrine prior to induction with propofol improves intubating conditions compared to propofol alone.

Keywords: Ephedrine, Saline, Group, Significant, Mean.

Introduction

Among the currently available non depolarizing neuromuscular blocking drugs for securing air ways, rocuronium complete the task around 60 – 90 seconds. Due to the slower onset at laryngeal muscles, around 20 – 25% patients, rocuronium didn't produce satisfactory intubating condition at a concetraton of 0.6 mg/Kg body weight. [1] Several modifications such as propofol, [1] priming either with rocuronium or mivacurium [2] or ephedrine in low doses along with intravenous induction agent [3] are recommended optimal intubating conditions at 60 seconds without changing the rocuronium dosage.

Access of neuromuscular blocker to muscle and its interaction with muscle nicotinic receptors is an important factor affecting the onset of action of neuromuscular blocking agents. The speed of a drug access to these receptors appears to be proportional to the cardiac output. [4] The effect of drugs affecting cardiac output and circulation time (ephedrine and esmolol) on the modulation of onset time of rocuronium have been documented. [5]

In addition the drug ephedrine has been shown to reduce the variability of onset of non depolarizing agents at the laryngeal muscle. This drug may also reduce the hypotension following propofol administration. With this, a study was taken to find the influnece of pre treatment of a low dose of intravenous ephedrine 70 µg/kg given prior to intravenous propofol, a commonly used induction agent in the dose of 2.5 mg/kg and rocuronium bromide in the dose of 0.6 mg/kg in improving the intubating conditions and its effects on haemodynamics during rapid tracheal intubation.

Methods

It was a prospective study conducted in the department of Anaethesiology, Rangaraya Medical College, Kakinada. Study was conducted between November 2016 and May 2018. The study protocol was approved by the Institutional Ethics Committee. Informed written consent was collected from the study participants.

Adults $\geq$ 18 years, who are on elective surgical procedures require general anaesthesia with tracheal intubation and controlled ventilation using musclerelaxant, weighing between 40 – 80 kgs, belong to American Society of Anesthesiology (ASA) grade I , II and Mallampati grade I and II were includede in this study. Pregnant women, known hypersensitivity to the study drugs, anticipated difficult airway, Mallampati Grade III, IV, who were on aminoglycosides, $MgsO_4$, ASA grade III, IV and those with cardio vascular, hepatic, renal impairment comorbid conditions were excluded.

All were premedicated with tab alprazolam 0.5 mg and tab ranitidine 150 mg orally at bed time the previous night of surgery. They were kept nil orally 10 pm onwards on the previous night. The study members were randomly divided into 2 groups; the group Ephedrine Rocuronium (ER) received ephedrine 70 µg/kg diluted to 5 ml with normal saline at the time of preoxygenation 3 min prior to laryngoscopy and intubation. Those includede in normal saline Rocuronium (NR) group received 5 ml normal saline at the time of preoxygenation 3 min prior to laryngoscopy and intubation. Routine pre-anaesthetic examination was conducted as per the insititutinal guidelines.

In the operation theatre, they were connected to to multi parameter monitor to record non invasive paramenets. An 18 G intravenous cannula was inserted to left

upper limb and infusion of ringer lactate was started. After recording the baseline reading, all were administered Midazolam 1 mg intravenously. They were preoxygenated for 3 minutes via a face mask with Bain's circuit. As per the protocol, either ER or NR was adminstered. After 1 minute, both groups were induced with intravenous Propofol 2.5 mg/kg with preservative free lidocaine 2%, 1ml for every 10 ml of propofol, injected over 30 seconds. One minute later, intravenous Rocuronium was given at 0.6 mg/kg and mask oxygenation was continued.

Sixty seconds after the administration of rocuronium, senior anaesthetist was asked to perform laryngoscopy and intubation with an appropriate sized Macintosh blade. He/she assessed the intubating conditions according to the scoring system as per Helbo Hansen et al. [6] Various study parameters such as heart rate (HR), blood pressuere (BP) and so on were recordede in the proforma. Time of intubation, duration of laryngoscopy, were also recorded. Care was taken to avoid any stimulus during the study period after intubation.

Statistical analysis: Data was analysed using SPSS version 22. T test, repeated measure ANOVA were used to find the statistiucal differece. $P < 0.05$ was considered to be statically signifcant.

Results

Total 120 (100%) members were included in this research, 60 (50%) in each group; male female ratio was 1 (Table 1).

Table 1: Genderwise distribution of study participants in the groups; n (%)

Gender	Groups		Total
	ER	NR	
Male	36 (30)	25 (21)	61 (51)
Female	24 (20)	35 (29)	59 (49)
Total	60 (50)	60 (50)	120 (100)
Mean age	27.6±6.302	28.10±6.048	-

Statistically there was no significant difference in the gender (P = 0.072) or age (P = 0.09). In ER group, intubating conditions were excellent for 42.5% (51) and good for 7.5% (9); whereas it was 35% (42), 11% (13) in NR group, respectively; statically there was significant difference (P = 0.003) (Table 2).

Table 2: Overall assessment of intubating conditions among the study members; n (%)

Rating	ER	NR	Total
Excellent	51 (42.5)	42 (35)	93 (77.5)
Good	9 (7.5)	13 (11)	22 (18.5)
Fair	0	5 (4)	5 (4)
Poor	0	0	0
Total	60 (50)	60 (50)	120 (100)

For laryngoscopy, the mean durations were 11.44±2.894 and 11.50±3.559 sec respectively for ER and NR groups; statistically there was no significant difference (P=0.926); whereas the mean intubation time was 18.18±3.095 sce and 19.50±6.914 sec respectively; statistically there was no significant difference (P=0.221). Statistically there was no significant difference in the base line HR between the groups. Whereas there was increase in HR immediately after administration of ephedrine and 1 minute after intubation; statically there was significant difference (Table 3).

Table 3: Comparison of mean heart rate (in beats/min) changes between the groups

Time	ER	NR	P value
Baseline	86.3200±11.42579	86.8000±13.88142	0.851
Ephedrine/ Saline	90.8±9.80629	86.28±10.98243	0.032
Postintubation 1	134.2200±15.10411	119.5000±15.34933	0.000

The baseline systolic blood pressure (SBP) was comparable between the groups; statitically not significant (P=0.178). In NR group, there was fall in SBP after propofol administration, increase at intubation; Whereas, in ER group, there was rise after ephedrine administration, after rocuronium and at intubation; statistically there was significant difference (P=0.000) (Table 4).

Table 4: Comparison of mean systolic blood pressure (SBP) changes between the groups.

Time	ER	NR	P value
Baseline	117.14±12.81	120.2±9.52	0.178
Ephedrine/ Saline	125.28±13.04	115.82±11.908	0.00
Propofol	109.74±14.91	102.72±12.57	0.012
Rocuronium	114.4 ± 12.10	103.34±10.97	0.00
Intubation	120.28 ± 20.35	135.92±20.52459	0.00

The baseline diastolic blood pressure (DBP) was comparable between groups; statitically not significant (P=0.226). In NR group, there was drop in DBP after propofol administration, and an increase at intubation and 1 min after intubation. Whereas, in ER group, DBP was raised at intubation 1 min and 2 min after intubation; statitically there was significant difference (Table 5).

Table 5: Comparison of mean diastolic blood pressure (DBP) changes between the groups.

Time	ER	NR	P value
Baseline	70.84 ± 14.8274	73.86 ± 9.31317	0.226
Propofol	66.02 ± 13.98613	66.12 ± 10.73929	0.968
Intubation	74.06 ±21.26165	88.5 ± 18.8553	0.001
Postintubation 1	74.9 ± 15.30939	88.06 ± 17.59802	0.000
Postintubation 2	72.14 ± 15.5314	85±15.36096	0.000

The baseline mean arterial pressure (MAP) was comparable; but there was no significant difference (P=0.357). There was fallin MAP after propofol administration in NR group and increased at intubation, 1 min after. In ER group, there was raise in mean MAP at intubation, 1 minute after; statistically there was significant difference (P<0.01) (Table 6).

Table 6: Comparison of mean arterial pressure (MAP) changes between the groups.

Time	ER	NR	P value
Baseline	86.4 ± 12.09655	88.38 ± 9.07765	0.357
Propofol	80.54 ± 11.97312	78.34 ± 10.58225	0.333
Intubation	89.46 ± 18.033.09	107.72 ± 16.76128	0.000
Postintubation 1	94.1 ± 13.83171	102.18 ± 17.34487	0.012

Discussion

In the present study, ephedrine at 70 µg/kg concentration was used; similar concentration of was reported. [4, 5, 7, 8] However, fixed dosage of ephedrine without considering the body weight was also reported by the investigators but there was no substantiated evidence with neuromuscular monitoring. Different concentrations of ephedrine, 30, 70 and 110 µg per kg body weight were also used by Kim et al., and Gopalakrishna et al. [3] Since 110 µg per kg body weight was reported to be associated with marked hypertension and tachycardia after intubation and there was no improvement of intubation conditions with 30 µg. [9]

Researchers [8, 5, 4] evaluated the effect of ephedrine 30 secs prior to the induction agent, reported that there was peak output at 1 – 2 mnts. Gopalakrishna et al. [3] also concluded that effect of ephedrine given 1 min before induction agent on the effect of rocuronium. Withthese, in this study, ephedrine was administered after preoxygenation for 3 minutes, 1 min before the administration of induction agent. Rocuronium was administered 1 min after the induction agent and laryngoscopy was done 60 secs later. Hence ephedrine was given 2 min prior to rocuronium bromide. Opioids were reported to be the induction agents, [1, 10] but omitted in the present study as our object was to find the effect of pretreatment with ephedrine on the intubating conditions.

Neuromuscular monitoring to find the onset of neuromuscular block was not done in this research. [11, 12] As per the available literature, the intubating conditions were graded as excellent, good, fair and poor; amomng these, excellent and good are clinically acceptable. [7, 8, 13, 14] However some investigatirs didn't use scoring system. [15] In this research, 42.5% (51) were excellent and 7.5% (9) were rated to be good in ER group, whereas it was 35% (42), 11% (13) in NR group, respectively; statically there was significant difference (P = 0.003) (Table 2). Tan et al. [7] also concluded that clinically acceptable intubating conditions were present among those in ER group. However, the proportion of excellent intubating conditions was significantly higher in the propofol ephedrine group (84%) compared to the propofol group (32%).

The basline mean HR was comparable in groups, respectively (86.32 vs 86.8 bpm). Statistically significant increase in mean HR in the ER group after administration (90.8 bpm); this was not observed in the NR group (86.28 bpm). The HR fell marginally (86.26 bpm) after administration of propofol in the ER group and to 80.54 bpm in the control group, which was statistically significant. HR fall was observed between the groups during administration of rocuronium, 1 min after propofol. However 1 min after tracheal intubation significant levels. The post intubation tachycardia persisted in both the groups till the end of the study group; this was statistically not significant. Gopalkrishna et al observed that there was statistically significant increase in the HR thise those received 75 and 150 µg/kg of ephedrine compared to the saline group and this persisted till the end of the study period. Also there was statistically significant difference in mean arterial pressure between groups. However in their study, considering 20% deviation from the baseline as clinically significant, all the groups were comparable during the first 5 minutes afterintubation. [16]

The basline SBP, DBP, MAP were comparable in groups. The baseline SBP were comparable between the groups; statitically not significant (P=0.178). In NR group, there was fall in SBP after propofol administration, increase at intubation; Whereas, in ER group, there was rise after ephedrine administration,

after rocuronium and at intubation; statistically there was significant difference (P=0.000) (Table 4). The baseline DBP was comparable between groups; statitically not significant (P=0.226). In NR group, there was drop in DBP after propofol administration, and an increase at intubation and 1 min after intubation. Whereas, in ER group, DBP was raised at intubation 1 min and 2 min after intubation; statitically there was significant difference (Table 5). In 1996 Gamlin et al., [17] studied the haemodynamic effects of propofol-ephedrine combination in healthy patients; there was significant decrease in both SBP (P<0.001) and DBP (P=0.003) among those received propofol alone. Also reported that the addition of ephedrine 15 mg or 20 mg to 1% propofol 20 ml was very effective in maintaining BP at pre-induction values. There was a statistically significant increase from baseline in SBP (P=0.004) and DBP (P=0.031), but this only occurred at 1 minute post induction. The addition of ephedrine 10 mg was insufficient to prevent hypotension. There was no significant effect on either heart rate or oxygen saturation in any group. They concluded that ephedrine may be safely employed to reduce the degree of hypotension during induction with propofol in this patient group.

The baseline MAP were comparable in both groups; but there was no significant difference (P=0.357). There was fall in MAP after propofol administration in NR group and an increase at intubation and 1 min after intubation. In ER group, there was raise in mean MAP at intubation and 1 minute after intubation; statistically there was significant difference (P<0.01) (Table 6). Tan et al. [7] adminstred fixed dose of ephedrine, 15 mg added to propofol 2.5 mg kg-1, found that there was significant increase in the HR and MAP in the propofol ephedrine group. Ganidagli et al. [18] also reported that there significant rise in MAP after administration of ephedrine. [19]

Conclusions

Pretreatment with Ephedrine hydrochloride 70 µg/kg prior to induction with propofol 2.5 mg/kg provides better intubating conditions and clinically there was no elevation in SBP, DBP and MAP.

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