A study of intubating conditions and haemodynamic characteristics using propofol and rocuronium after pre-treatment with ephedrine

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Abstract

Background and Objectives: The present study was conducted to compare the efficacy of Pre-treatment with a low dose of intravenous ephedrine 70 µg kg-1 on the intubating conditions and its effects on hemodynamic during rapid tracheal intubation using propofol 2.5 mg kg-1 and rocuronium bromide 0.6 mg kg-1.

Methodology: In this study one hundred patients were included and randomly divided into two equal groups which received either ephedrine 70 µg kg^{-1} diluted to 5 ml with normal saline (Group EPR) or 5 ml of normal saline (Group SPR) 3 min prior to laryngoscopy and intubation with Propofol 2.5 mg kg^{-1} and rocuronium bromide 0.6 mg kg^{-1}. A blinded anaesthesiologist assessed the intubating conditions; heart rate and mean arterial pressure before anaesthesia induction (baseline), and every minute thereafter till5 minutes post intubation. A 30% change in hemodynamic variables from baseline was regarded as clinically significant. Data were analyzed using Paired samples t-test.

Results: Intubating conditions were better (p=0.023) in the ephedrine pre-treated group. There was no statistically significant difference between the ephedrine pre-treated group and control regarding the time taken for laryngoscopy and intubation. There were no significant hemodynamic changes between the two groups except tachycardia.

Conclusion: Ephedrine 70 µg kg^{-1} prior to induction with propofol 2.5 mg kg^{-1} improves intubating conditions compared to propofol alone 1 minute after 0.6 mg kg^{-1} rocuronium bromide injection without significant hemodynamic effects.

Key Words: Ephedrine; Rocuronium; Propofol; Rapid tracheal intubation.

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Introduction

The primary concern of the anaesthesiologist in several emergent clinical situations is to secure the airway. This can be done in an awake patient by laryngoscopy and placement of an endotracheal tube. The ease of endotracheal intubation can be enhanced by using an appropriate neuromuscular blocking agent but this puts the patient under the risk of developing apnoea, loss of protective airway reflexes, regurgitation and pulmonary aspiration of stomach contents. Succinylcholine is a depolarizing neuromuscular blocking agent with a rapid onset and short duration of action with profound neuromuscular blockade. The use of succinylcholine can however be associated with many side effects including muscular pains, bradycardia, increased plasma potassium concentration and raised intra-ocular pressure. Amongst the currently available non depolarizing neuromuscular blocking drugs, rocuronium in a dose of 2 X ED95 (0.6 mg/kg) or 3 X ED95 (0.9 mg/kg) has the most rapid onset of action, taking about 60-90 seconds for complete block to develop and may be an alternative to succinylcholine. However larger doses tend to prolong the duration of action which is undesirable, But rocuronium 0.6 mg/kg is claimed not to produce satisfactory intubating conditions at 60 seconds in 20-25% of the patients[1].

Ephedrine is an indirectly acting synthetic non catecholamine having an agonistic action on both alpha and beta-adrenergic receptors. It acts by directly stimulating the adrenergic receptors and indirectly by enhancing the endogenous release of norepinephrine.

The effects on the cardiovascular system resemble those of epinephrine but the elevation of systemic blood pressure is less intense and lasts approximately ten times longer.

On intravenous administration there is an increase in systolic as well as diastolic blood pressure, heart rate and cardiac output. It decreases the renal and splanchnic blood flow but there is an increase in the coronary blood flow and the blood flow to skeletal muscles. Minimal change is seen in systemic vascular resistance.

Ephedrine is commonly used drug to increase systemic blood pressure in the presence of sympathetic nervous system blockade produced by regional anaesthesia or hypotension due to inhaled or injected anaesthetics. In addition to its alpha vasoconstrictive action and beta cardiac stimulant effect, ephedrine also has the added advantage of having a similar action profile as propofol.[2] The peak onset of propofol is known to occur between 2-3 minutes. However, the peak effect of ephedrine on blood pressure is 2 minutes, slightly

earlier than propofol. The use of propofol has several potential advantages that can achieve the major objectives of a rapid tracheal induction technique. The faster onset of action, potent attenuation of pharyngeal, laryngeal and tracheal reflexes and adequate depth of anaesthesia during intubation are among these.[3]

Materials and Methods

Present study was undertaken in National Institute of Medical Sciences and Hospital, Jaipur during the period January 2014 and May 2015. The study was undertaken after obtaining approval of Institutional Ethical Committee as well as informed written consent from all patients who were included in the study.

Inclusion Criteria

1. Normal adult patients aged between 20 yrs – 40 yrs.
2. Patients weighing between 50 kgs – 70 kgs.
3. Patients belonging to ASA physical status I and II.
4. Mallampati grades I and II.
5. Elective surgical procedures requiring general anaesthesia with tracheal intubation and controlled ventilation using muscle relaxant.

Exclusion Criteria

1. Patients <20 years and >40 years.
2. Patients with ASA physical status > III.
3. Mallampati grade III and IV.
4. Patients with hypertension, ischaemic heart disease, cerebrovascular disease, diabetes mellitus, pheochromocytoma, respiratory tract pathology or at risk of regurgitation, aspiration (previous upper gastrointestinal tract surgeries, known or symptomatic hiatus hernia, oesophageal reflux, peptic ulceration or full stomach).
5. Emergency surgical procedures.
6. Patients with known difficult airway.
7. History of known allergy to drugs used in the study.
8. Pregnancy.

Study Methods

In this present study 100 ASA physical status I and II adult patients, aged between 20 and 40 years, posted for various elective surgeries under general anaesthesia, were selected on the basis of a simple random sampling method. Detailed pre anaesthetic evaluation was performed on the day before the surgery. Airway evaluation was done with Mallampati grading and measurement of thyromental distance. Informed written consent from the patient was taken for the study and anaesthesia as well. Age and weight of the patients were recorded.

The study population was randomly divided using simple sealed envelope method into two groups, with 50 patients in each group: Group EPR (Ephedrine Propofol Rocuronium) and Group SPR (Saline Propofol Rocuronium).

Patients in Ephedrine Propofol Rocuronium group received ephedrine 70μg/kg diluted to 5 ml with normal saline at the time of pre-oxygenation 3 min prior to laryngoscopy and intubation.

Patients in Saline Propofol Rocuronium group received 5 ml of normal saline at the time of pre-oxygenation 3 min prior to laryngoscopy and intubation. A routine pre-anaesthetic examination was conducted assessing:

- General condition of the patient
- Airway assessment by Mallampati grading and rule of 1-2-3
- Nutritional status and weight of the patient
- A detailed examination of the cardiovascular system
- A detailed examination of the respiratory system

The following investigations were done in all patients.

- Haemoglobin estimation
- Urine examination for albumin, sugar and microscopy
- Standard 12- lead electrocardiogram
- X-ray chest/ Screening of chest
- Blood sugar, FBS/PPBS
- Blood urea, Serum creatinine

All patients included in the study were pre-medicated with tab alprazolam 0.5 mg and tab ranitidine 150 mg orally at bed time the previous night before surgery. They were kept nil orally 10 pm onwards on the previous night.

Methods of Collection of Data

On arrival in the Operation theatre, patients were connected to multi parameter monitor (Star plus of Larsen & Toubro) which records heart rate, noninvasive measurements of systolic blood pressure, diastolic blood pressure, mean arterial pressure, $EtCO_2$ and continuous ECG monitoring and oxygen saturation. The baseline heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressures and SpO_2 were recorded. The cardiac rate and rhythm were also monitored from a continuous visual display of electrocardiogram from lead II. An 18 G intravenous cannula was inserted into left upper limb and an infusion of ringer lactate started.

An anaesthesiologist uninvolved in the present study was asked to prepare a 5 ml unlabelled syringe containing either 5 ml normal saline or ephedrine 70 μg/kg diluted to 5 ml with normal saline.

The patients were randomly allotted into two groups: Group EPR (Ephedrine Propofol Rocuronium) and SPR (Saline Propofol Rocuronium). After recording the baseline reading, all patients were administered Inj. Midazolam 1 mg intravenously slowly. All patients were pre-oxygenated with 100% O_2 for 3 minutes.

Patients in Ephedrine Propofol Rocuronium group received ephedrine 70 μg/kg diluted to 5 ml of normal saline at the time of pre-oxygenation while patients in Saline Propofol Rocuronium group received 5 ml of

normal saline. After 1 minute, patients in both the 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 after Propofol, patients in both the groups were given intravenous Rocuronium 0.6 mg/kg and mask ventilation continued with 100% O_2. Sixty seconds after the administration of rocuronium, an anaesthesiologist (Observer 1) who had more than 3 years of experience and was blinded to the study drug was asked to perform laryngoscopy and intubation with an appropriate sized Macintosh blade. He/she assessed the intubating conditions according to the scoring system suggested by Cooper et al. (Table 1). Cuffed Oral endotracheal tube (PORTEX®) of size 7.0 mm ID for female patients and 8.5 mm ID for male patients was used for intubation and cuff inflated till the disappearance of palpable leak on positive pressure ventilation. Patients with Cormack–Lehanne grading of laryngoscopy 3 or 4 were e excluded from further analysis. The duration of laryngoscopy and time for intubation were also recorded (Observer 2) during pre-induction (baseline), just before intubation and every minute thereafter for 5 minutes. 30% change in hemodynamic variables from the baseline value was regarded as significant and managed by the concerned anaesthesiologist as per his/her discretion.

The time for intubation (number of seconds from the first contact of the intubator to successful placement of endotracheal tube); duration of laryngoscopy (time from insertion of the laryngoscope blade into the patient's mouth to its removal after successful intubation); reaction for the endotracheal intubation, was recorded by the anaesthesiology resident, the primary investigator of the study. Anaesthesia was maintained with 33% oxygen, 67% nitrous oxide at fresh gas flow of 6 liters/minute after intubation, with positive pressure ventilation using Bain's circuit. Care was taken to avoid any stimulus during the study period after intubation. The patient was then followed up intra operatively and post operatively for 24 hours.

Monitoring

The following cardiovascular parameters were recorded in all patients.

- Heart rate [HR] in beats per minute.
- Systolic blood pressure [SBP] in mm of Hg
- Diastolic blood pressure [DBP] in mm of Hg
- Mean arterial pressure [MAP] in mm of Hg
- SpO_2 in percentage.

The above cardiovascular parameters were mentioned in the following time interval –

1. Basal before giving study drug.
2. Pre induction: after giving premedication, start of pre-oxygenation.
3. During pre-oxygenation at the end of 1st and 2nd minute
4. 3rd minute of pre-oxygenation, after the study drug.
5. After induction with propofol.
6. 1 minute after propofol, rocuronium 0.6 mg/kg.
7. During laryngoscopy/intubation.
8. After laryngoscopy and intubation, every minute thereafter for the next five minutes.
9. Hypotension was defined as SBP < 30% of baseline value or 90 mmHg, which ever was lower.
10. Hypertension was defined as SBP > 30% of baseline value or 150 mmHg, which ever was higher.
11. Tachycardia was defined as HR > 25% of baseline value.
12. Bradycardia was defined as HR < 60 beats/ minute.
13. Any dysrrhythmia was defined as any ventricular or supra ventricular beat or any rhythm other than sinus.

Results

A study entitled "A Study of Intubating Conditions and Haemodynamic Characteristics using Propofol and Rocuronium after Pre Treatment with Ephedrine" was undertaken in National Institute of Medical Sciences and Hospital, Jaipur from January 2014 to May 2015. A total of 100 patients were studied, 50 in each group. None of the patients were excluded from the study.

Table 1: The age distribution

Age (in Years)	Group EPR (Ephedrine)		Group SPR (Control)	
	Number of Patients (n)	Percentage (%)	Number of Patients (n)	Percentage (%)
20-25	11	22 %	13	26 %
26-30	11	22 %	12	24 %
31-35	9	18 %	8	16 %
36-40	19	38 %	17	34 %
Total	50	(100)	50	(100)
Mean Age in Yrs ± SD	32.02+6.744		31.04+7.111	
P value	0.481			

Table 1 shows age distribution of the patients in both the groups. The minimum age in groups Ephedrine Propofol Rocuronium and Saline Propofol Rocuronium was 20 years. The maximum age in both groups was 40 years. The

mean age in group Ephedrine Propofol Rocuronium and Saline Propofol Rocuronium were 32.02±6.744yrs and 31.04±7.111 years respectively. There was no significant difference (p= 0.481) in the age of patients between the Group Ephedrine Propofol Rocuronium and Group Saline Propofol Rocuronium.

Table 2: Sex Distribution between Group EPR and Group SPR

		Groups		Total
		EPR n (%)	SPR n (%)	
Sex	Male	18 (36)	17 (34)	35 (35)
	Female	32 (64)	33(66)	65(65)
Total		50 (100)	50 (100)	100

Table 2 shows that there is no statistically significant difference in the gender in both the groups (p=0.072).

Table 3: Body weight and height distribution

	Group	N	Mean	Std. Deviation	P value
Height (cms)	EPR	50	162	3.462	0.764
	SPR	50	161.7	6.126	
Weight (Kgs)	EPR	50	57	7.2	1.000
	SPR	50	57	9.3	

Table 3 shows the mean body weight and height of the patients. The minimum body weight in groups Ephedrine Propofol Rocuronium and Saline Propofol Rocuronium was 48 kg & maximum body weight was 86 kg. The mean body weight in Group Ephedrine Propofol Rocuronium was 57±7.2 kgs and in Group Saline Propofol Rocuronium it was 57±9.3 kg. The mean height in Group Ephedrine Propofol Rocuronium was 162±3.462 cms and in Group Saline Propofol Rocuronium it was 161.7±6.126 cms. There was no significant difference in the height & body weight of patients between the Group Ephedrine Propofol Rocuronium and Group Saline Propofol Rocuronium (p=0.764) & (p= 1.000) respectively.

Table 4: The distribution of assessment of jaw relaxation

		Group		P Value
		EPR n (%)	SPR n (%)	
Jaw Relaxation	Easy	49 (98)	46 (92)	0.83
	Fair	1 (2)	3 (6)	0.265
	Difficult	0 (0)	1 (2)	1.00
Total		50 (100)	50 (100)	

Table 4 shows the patient distribution with regard to assessment of jaw relaxation for laryngoscopy among the two groups. Laryngoscopy was difficult in one of the patients in Saline Propofol Rocuronium group (patient No. 82). There is no statistical significance in assessment of jaw relaxation between the groups Ephedrine Propofol Rocuronium and Saline Propofol Rocuronium.

Table 5: The distribution of position of vocal cords during laryngoscopy

		Group	
		ERP n (%)	SRP n (%)
Vocal Cord	Open	45 (90)	43 (86)
	Moving	5 (10)	4 (8)
	Closing	0 (0)	2 (4)
	Closed	0 (0)	1 (2)
Total		50 (100)	50 (100)

Table 5 shows the patient distribution with regard to assessment of vocal Cord position and movement during laryngoscopy. During laryngoscopy, in the ephedrine pre-treated patients, vocal cords were open in all the patients. In the saline group, vocal cords were open in 43 (96%) patients; only one patient had closed vocal cords (patient No. 10) and two had closing vocal cords (patient Nos. 37 & 40) and four had moving vocal cords.

Table 6: The distribution of assessment of diaphragmatic movements during Laryngoscopy

		Group		P Value
		ERP n (%)	SRP n (%)	
Diaphragmatic Movements	None	26 (52)	20 (40)	0.110
	Slight diaphragmatic movements	16 (32)	13 (26)	
	Mild coughing	7 (14)	10 (20)	
	Severe coughing or Bucking	1 (2)	7 (14)	
Total		50 (100)	50 (100)	

Table 6 shows the patient distribution with regard to assessment of diaphragmatic movements during laryngoscopy. During laryngoscopy, in the ephedrine pre-treated patients, 35 (70%) had no diaphragmatic movements. 6 (12%) slight diaphragmatic movements, 6 (12%) mild coughing and 3 (6%) severe coughing or bucking. In the saline group, 20 (40%) patients had no response, 13 (26%) slight diaphragmatic movements, 10 (20%) mild coughing and 7 (14%) severe coughing or bucking. There is a statistical not significance between the two groups regarding the assessment of diaphragmatic movements (p=0.110)

Table 7: The distribution of overall assessment of intubating conditions

		group		P Value
		EPR n (%)	SPR n (%)	
Intubating Conditions	Excellent	42 (84)	32 (64)	0.023
	Good	8 (16)	13 (26)	
	Fair	0 (0)	5 (10)	
	Poor	0 (0)	0 (0)	
Total		50 (100)	50 (100)	

Table 7 shows the patient distribution with regard to assessment of overall intubation conditions. In the ephedrine pre-treated groups 42 (84%) had excellent and 8 (16%) had good intubating conditions compared to the saline pre-treated group [32 (64%) excellent, 13 (26%) good and 5 (10%) fair intubating conditions]. Statistically significant difference (p=0.023) was found between ephedrine pre-treated group and saline pre-treated group suggesting better intubating conditions in the ephedrine pre-treated group.

Table 8: The time taken for laryngoscopy and confirmation of successful intubation

		Group		P Value
		EPR n (50)	SPR n (50)	
Laryngoscopy	Mean duration±SD in seconds	11.48+2.915	11.5+3.558	0.975
Intubation Time	Mean duration±SD in seconds	18.2+3.083	19.5+6.914	0.227

Table 8 shows duration of laryngoscopy and confirmation of successful intubation after rocuronium administration with or without ephedrine pre-treatment (mean and standard deviation). There is no statistical significance between the groups EPR and SPR regarding duration of laryngoscopy (p=0.975) and duration of intubation time (p=0.227). The mean duration of the time taken for laryngoscopy and intubation time were comparable in both the groups.

Table 9: The inter-group comparison of Heart rate (in beats/min) changes in response to between EPR group and SPR group

Time	Group EPR	Group SPR	P value
Baseline	86.44+11.388	89+19.851	0.430
Midazolam	84.54+11.587	84.28+11.784	0.940
Pre oxygenation 1	84.06+11.654	84.48+10.436	0.849
Pre oxygenation 2	83.96+10.677	84.82+11.289	0.696
Pre oxygenation 3	84.5+10.278	85.78+11.354	0.555
Ephedrine/ Saline	90.46+9.908	86.28+10.982	0.048
Propofol	85.68+9.732	80.74+9.127	0.010
Rocuronium	86.84+8.601	81+8.871	0.001
Intubation	113.16+17.416	116.92+16.363	0.268
Post intubation 1	134.06+15.448	119.5+15.349	0.0001
Post intubation 2	119.78+14.635	118.38+15.184	0.639
Post intubation 3	113.2+15.643	117.08+15.307	0.213
Post intubation 4	110.44+16.018	114.58+16.558	0.206
Post intubation 5	108.26+14.617	110.34+16.754	0.013

($p<0.01$) – Highly significant (HS); ($p<0.05$) – Significant (S); ($p>0.05$) – Not significant (NS)

Table 10: The intergroup comparison of SBP (mm of Hg) changes in response to between EPR group and SPR group

Time	Group EPR	Group SPR	P value
Baseline	116.6+12.728	120.2+9.519	0.112
Midazolam	120.22+20.018	119.52+9.573	0.823
Pre oxygenation 1	116.6+12.728	116.58+9.623	0.992
Pre oxygenation 2	114.38+13.566	117.34+9.588	0.210
Pre oxygenation 3	112.8+10.757	116.54+10.333	0.079
Ephedrine/ Saline	124.7+13.316	116.06+11.218	0.0007
Propofol	110.2+15.215	102.72+12.565	0.008
Rocuronium	114.3+12.087	103.34+10.972	0.0001
Intubation	119.5+19.887	135.9+20.504	0.0001
Post intubation 1	133.12+18.929	129.4+20.386	0.356
Post intubation 2	122.1+13.453	121.34+18.189	0.812
Post intubation 3	116.76+9.434	116.8+17.161	0.988
Post intubation 4	118.02+11.390	115.44+17.275	0.380
Post intubation 5	114.42+9.521	113.84+14.719	0.815

Table 10 show that the basal systolic blood pressure were comparable in both groups (p=0.178). Statistical evaluation between the groups showed a statistically highly significant fall in systolic blood pressure in group Saline Propofol Rocuronium after propofol administration, increase at intubation. The mean systolic blood pressure increase observed after ephedrine administration, after rocuronium and at intubation in group Ephedrine Propofol Rocuronium was statistically significant compared to mean systolic blood pressure in group Saline Propofol Rocuronium (p=0.000).

Table 11: The inter-group comparison of DBP (in mm of Hg) changes in response to between EPR group and SPR group

Time	Group EPR	Group SPR	P value
Baseline	70.86+14.820	73.86+9.313	0.228
Midazolam	71.22+13.065	72.92+9.646	0.461
Pre oxygenation 1	69.62+14.471	70.46+10.654	0.741
Pre oxygenation 2	69.92+14.624	71.18+10.245	0.618
Pre oxygenation 3	68.92+14.276	71.1+10.037	0.379
Ephedrine/ Saline	69.12+14.985	73.16+9.575	0.111
Propofol	65.86+13.924	66.32+10.367	0.851
Rocuronium	66.38+13.277	67.48+11.187	0.655
Intubation	74.08+21.296	88.1+18.948	0.084
Post intubation 1	74.52+15.093	87.62+18.108	0.0002

Post intubation 2	72.94+15.607	84.06+14.577	0.0004
Post intubation 3	70.7+20.243	76.94+14.280	0.078
Post intubation 4	69.96+11.342	76.84+14.086	0.008
Post intubation 5	67.36+10.961	73.72+14.957	0.017

Table 11 shows that the basal diastolic blood pressure were comparable in both groups (p=0.226). Statistical evaluation between the groups showed a statistically not significant fall in diastolic blood pressure in group Saline Propofol Rocuronium after propofol administration, and an increase at intubation and 1 min after intubation. The mean diastolic blood pressure increase observed at intubation 1 min and 2 min after intubation in group Ephedrine Propofol Rocuronium was statistically significant compared to mean diastolic blood pressure in group Saline Propofol Rocuronium ($p<0.05$).

Table 12: The intergroup comparison of MAP (in mm of Hg) changes in response to between EPR group and SPR group

Time	Group EPR	Group SPR	p-value
Baseline	86.42+12.147	88.38+9.078	0.363
Midazolam	87.18+12.0182	87.56+19.841	0.908
Pre oxygenation 1	85.44+11.528	87.48+10.312	0.353
Pre oxygenation 2	84.64+11.840	88.5+8.115	0.060
Pre oxygenation 3	83.56+10.932	86.34+10.557	0.198
Ephedrine/ Saline	87.82+10.787	87.4+8.960	0.832
Propofol	80.56+11.952	78.14+10.567	0.286
Rocuronium	81.44+9.049	79.38+8.403	0.241
Intubation	89.48+18.073	107.72+16.761	0.0001
Post intubation 1	93.94+13.639	102.18+17.344	0.009
Post intubation 2	88.8+12.846	93.56+13.404	0.072
Post intubation 3	86.58+9.783	90.2+14.068	0.138
Post intubation 4	85.9+9.100	89.84+13.952	0.097
Post intubation 5	84.06+8.777	86.38+12.373	0.282

The basal MAP were comparable in both groups (p=0.357). Statistical evaluation between the groups showed a statistically highly significant fall in MAP in group SPR after propofol administration and an increase at intubation and 1 min after intubation. The mean MAP increase observed at intubation and 1 minute after intubation in group EPR was statistically highly significant compared to mean MAP in group SPR ($p<0.01$).

Table 13: The intra group comparison of mean heart rate (bpm) changes in EPR group compared to basal heart rate

Time	Group EPR	P value
Baseline	86.44+11.388	
Midazolam	84.54+11.587	0.410
Pre oxygenation 1	84.06+11.654	0.304
Pre oxygenation 2	83.96+10.677	0.264
Pre oxygenation 3	84.5+10.278	0.373
Ephedrine/ Saline	90.46+9.908	0.062
Propofol	85.68+9.732	0.720
Rocuronium	86.84+8.601	0.843
Intubation	113.16+17.416	0.0001
Post intubation 1	134.06+15.448	0.0001
Post intubation 2	119.78+14.635	0.0001
Post intubation 3	113.2+15.643	0.0001
Post intubation 4	110.44+16.018	0.0001
Post intubation 5	108.26+14.617	0.0001

In group EPR (ephedrine), the basal mean HR was 86.44±11.388 bpm. The mean HR after the study drug administration was 90.46±9.908 bpm which was highly significant. The mean HR after intubation was 113.16±17.416 bpm which was highly significant compared to baseline (p= 0.00). The increase in mean HR after intubation was statistically highly significant (p=0.000) compared to baseline HR. The mean HR remained above basal value even at 5 minutes after intubation

Table 14: The intra group comparison of mean heart rate (BPM) changes in SPR group compared to basal heart rate

Time	Group SPR	P value
Baseline	89+19.851	
Midazolam	84.28+11.784	0.151
Pre oxygenation 1	84.48+10.436	0.157
Pre oxygenation 2	84.82+11.289	0.198
Pre oxygenation 3	85.78+11.354	0.321
Ephedrine/ Saline	86.28+10.982	0.144
Propofol	80.74+9.127	0.008
Rocuronium	81+8.871	0.010
Intubation	116.92+16.363	0.0001
Post intubation 1	119.5+15.349	0.0001
Post intubation 2	118.38+15.184	0.0001
Post intubation 3	117.08+15.307	0.0001
Post intubation 4	114.58+16.558	0.0001
Post intubation 5	110.34+16.754	0.0001

In group SPR (control), the basal mean HR was 89±19.851 bpm. The mean HR after the administration of propofol was 80.74±9.127 bpm which was statistically significant (p=0.000). The mean HR just after intubation was 116.92±16.363 bpm which was statistically highly significant (p= 0.000). The mean HR remained above basal value at intubation and even at 5 minutes after intubation.

Table 15: The intra-group comparison of mean SBP (mm of Hg) changes in EPR group compared to basal SBP

Time	Group EPR	P value
Baseline	116.6+12.728	
Midazolam	120.22+20.018	0.283
Pre oxygenation 1	116.6+12.728	1.000
Pre oxygenation 2	114.38+13.566	0.400
Pre oxygenation 3	112.8+10.757	0.110
Ephedrine/ Saline	124.7+13.316	0.002
Propofol	110.2+15.215	0.024
Rocuronium	114.3+12.087	0.356
Intubation	119.5+19.887	0.387
Post intubation 1	133.12+18.929	0.0001
Post intubation 2	122.1+13.453	0.038
Post intubation 3	116.76+9.434	0.943
Post intubation 4	118.02+11.390	0.558
Post intubation 5	114.42+9.521	0.334

In group EPR (ephedrine), the basal mean SBP was 116.6±12.728 mm Hg. The mean SBP after administration of ephedrine was 124.7±13.316 which was highly significant (p=0.002). The mean SBP after the administration of propofol was 110.2±15.215 mm Hg which was statistically significant (p<0.024). The mean SBP 1 min after intubation was 133.12±18.929 mm Hg which was highly significant compared to baseline (p= 0.00). The mean SBP just after intubation was 119.5±19.887 mm Hg representing an increase of 3.1 mm Hg from the basal SBP which was statistically not significant (p> 0.005). The mean SBP at 2, 3, 4 and 5 minutes after intubation were statistically not significant (p >0.05) compared to baseline SBP.

Table 16: The intra-group comparison of mean SBP (mm of Hg) changes in SPR group compared to basal SBP

Time	Group SPR	P value
Baseline	120.2+9.519	
Midazolam	119.52+9.573	0.825
Pre oxygenation 1	116.58+9.623	0.242
Pre oxygenation 2	117.34+9.588	0.351
Pre oxygenation 3	116.54+10.333	0.244
Ephedrine/ Saline	116.06+11.218	0.196
Propofol	102.72+12.565	0.0001
Rocuronium	103.34+10.972	0.0001
Intubation	135.9+20.504	0.0002
Post intubation 1	129.4+20.386	0.023
Post intubation 2	121.34+18.189	0.763
Post intubation 3	116.8+17.161	0.357
Post intubation 4	115.44+17.275	0.199
Post intubation 5	113.84+14.719	0.068

In group SPR (control), the basal mean SBP was 120.2±9.519 mm Hg. The mean SBP after the administration of propofol was 102.72±12.57 mm Hg which was highly significant (p=0.000). The mean SBP 1 min after propofol and after intubation was 102.72±12.565 and 135.9±20.504 mm Hg which was highly significant compared to baseline (p= 0.00). By 2nd and 3rd min after intubation the mean SBP were 121.34±18.189 and 116.8±17.161 mm Hg respectively which were statistically not significant (p >0.05) compared to baseline SBP. The mean SBP 4 and 5 min after intubation was significant. (p<0.005)

Table 17: The intra-group comparison of mean DBP (mm of Hg) changes in EPR group compared to basal DBP

Time	Group EPR	P value
Baseline	70.86+14.820	
Midazolam	71.22+13.065	0.897
Pre oxygenation 1	69.62+14.471	0.673
Pre oxygenation 2	69.92+14.624	0.750
Pre oxygenation 3	68.92+14.276	0.506
Ephedrine/ Saline	69.12+14.985	0.560
Propofol	65.86+13.924	0.085
Rocuronium	66.38+13.277	0.114
Intubation	74.08+21.296	0.382
Post intubation 1	74.52+15.093	0.224
Post intubation 2	72.94+15.607	0.496
Post intubation 3	70.7+20.243	0.964
Post intubation 4	69.96+11.342	0.733
Post intubation 5	67.36+10.961	0.182

In group EPR (ephedrine), the basal mean DBP was 70.86±14.820 mm Hg. The mean DBP after the administration of propofol was 65.86±13.924 mm Hg and rocuronium was 66.38±13.277 which was significant (p<0.005). The mean DBP 1 min after intubation was 74.52 ± 15.093 mm Hg which was not significant compared to baseline (p> 0.005). The mean DBP 2, 3, 4 and 5 minutes after intubation were statistically not significant (p >0.05) compared to baseline DBP.

Table 18: Showing the intra group comparison of mean DBP (mm of Hg) changes in SPR group compared to basal DBP

Time	Group SPR	P value
Baseline	73.86+9.313	
Midazolam	72.92+9.646	0.621
Pre oxygenation 1	70.46+10.654	0.092
Pre oxygenation 2	71.18+10.245	0.174
Pre oxygenation 3	71.1+10.037	0.157
Ephedrine/ Saline	73.16+9.575	0.711
Propofol	66.32+10.367	0.0002
Rocuronium	67.48+11.187	0.002
Intubation	88.1+18.948	0.0001
Post intubation 1	87.62+18.108	0.0001
Post intubation 2	84.06+14.577	0.0001
Post intubation 3	76.94+14.280	0.204
Post intubation 4	76.84+14.086	0.215
Post intubation 5	73.72+14.957	0.955

In group SPR (control), the basal mean DBP was 73.86 ± 9.313 mm Hg. The mean DBP after the administration of propofol was 66.32±10.367 mm Hg which was highly significant (p=0.000). The mean DBP after rocuronium and intubation were highly significant compared to baseline (p= 0.00). By 3, 4 and 5 minutes the mean BP were 76.94±14.280, 76.84±14.086 and 73.72±14.957 mm Hg respectively which were statistically not significant (p>0.05) compared to baseline DBP.

Table 19: Showing the intra group comparison of MAP (mm of Hg) changes in EPR group compared to basal MAP

Time	Group EPR	p-value
Baseline	86.42+12.147	
Midazolam	87.18+12.0182	0.753
Pre oxygenation 1	85.44+11.528	0.679
Pre oxygenation 2	84.64+11.840	0.459
Pre oxygenation 3	83.56+10.932	0.218
Ephedrine/ Saline	87.82+10.787	0.543
Propofol	80.56+11.952	0.016
Rocuronium	81.44+9.049	0.022
Intubation	89.48+18.073	0.322
Post intubation 1	93.94+13.639	0.004
Post intubation 2	88.8+12.846	0.343
Post intubation 3	86.58+9.783	0.942
Post intubation 4	85.9+9.100	0.809
Post intubation 5	84.06+8.777	0.268

In group EPR (ephedrine), the basal mean arterial pressure (MAP) was 86.42±12.147 mm Hg. The mean MAP after the administration of propofol was 80.56±11.952 mm Hg which was highly significant (p=0.000) and rocuronium was 81.44±9.049 mm Hg which was significant. The mean MAP 1 min after intubation was 93.94±13.639 mm Hg which was highly significant compared to baseline (p=0.004). The mean MAP just after intubation was 89.48±18.073 mm Hg representing an increase of 3.2 mm Hg from the basal MAP which was statistically not significant (p> 0.005). By 3,4 and 5 minutes after intubation the mean MAP were 86.58±9.783, 85.9±9.100 and 84.06±8.777 mm Hg respectively which were statistically not significant (p >0.05) compared to baseline MAP.

Table 20: Showing the intra group comparison of MAP (mm of Hg) changes in SPR group compared to basal MAP

Time	Group SPR	P value
Baseline	88.38+9.078	
Midazolam	87.56+19.841	0.791
Pre oxygenation 1	87.48+10.312	0.644
Pre oxygenation 2	88.5+8.115	0.944
Pre oxygenation 3	86.34+10.557	0.302
Ephedrine/ Saline	87.4+8.960	0.588
Propofol	78.14+10.567	0.001
Rocuronium	79.38+8.403	0.0001
Intubation	107.72+16.761	0.0001
Post intubation 1	102.18+17.344	0.0001
Post intubation 2	93.56+13.404	0.025
Post intubation 3	90.2+14.068	0.443
Post intubation 4	89.84+13.952	0.536
Post intubation 5	86.38+12.373	0.359

In group SPR (control), the basal mean arterial pressure (MAP) was88.38±9.08 mm Hg. The mean MAP after the administration of propofol was78.14±10.567 mm Hg which was highly significant (p=0.001). The mean MAP after rocuronium and intubation was highly significant compared to baseline (p=0.00). By 2 minutes after intubation the mean MAP was 93.56±13.404 which was significant (p=0.025). By 3, 4 and 5 minutes the mean MAP were 90.2±14.068, 89.84±13.952 mm Hg and 86.38±12.373 mm Hg respectively which were statistically not significant (p>0.05) compared to baseline MAP.

Discussion

In several emergent clinical situations the primary concern of the anaesthesiologist is to secure the airway. In an awake patient it can be done by Laryngoscopy and placement of an endotracheal tube but it is not a comfortable option both for the patient and the anaesthesiologist. Induction and paralysis with a neuromuscular blocking agent is highly useful to achieve endotracheal intubation. But there are chances of apnoea, loss of protective airway reflexes, regurgitation and pulmonary aspiration of stomach contents. Therefore, adequate oxygenation before induction and administration of a neuromuscular blocking drug (rapid onset and short duration) and application of cricoid pressure till a cuffed oral endotracheal tube is placed, are the measures universally followed in such 'rapid sequence induction'.

Traditionally, thiopentone sodium as inducting agent and succinylcholine as neuromuscular blocking agent are used in rapid tracheal intubation. Succinylcholine as a depolarizing neuromuscular blocking agent has a rapid onset (50±17 sec), short duration of action (9±2 minutes) and profound neuromuscular paralysis/relaxation. Many Neuromuscular monitoring studies have shown that its action at the vocal cords (50±11 sec) is earlier at adductor pollicis muscle (80±24 sec).[41] Rapid onset, easy laryngoscopy, vocal cord paralysis and jaw relaxation make succinylcholine the gold standard in rapid tracheal intubation. But on the other hand succinylcholine has several disadvantages like increased intracranial pressure, intragastric and intraocular pressure, myalgias, masseter spasm, cardiac dysrhythmias, sinus bradycardia, nodal rhythms, ventricular dysrhythmias and hyperkalemia.

Succinylcholine is contraindicated in patients with major crush injuries (over 48 hours), major burns (over48 hours), severe abdominal sepsis, denervation syndromes, and major nerve or spinal cord injuries due to the risk of hyperkalemia which may lead to fatal cardiac arrhythmia. Succinylcholine is also contraindicated in patients with a history of malignant hyperthermia or previous allergic reaction to it. The depolarising action of succinylcholine at neuromuscular junction is non physiological. Therefore, there is a search for an alternative neuromuscular blocking agent to succinylcholine in rapid tracheal intubation which is non-depolarizing and has a rapid onset of action at the neuromuscular junction, with good intubating conditions and a short duration of action. From the other non-depolarizing neuromuscular blocking agents available, due to low potency as compared to other non-depolarizing agents like pancuronium bromide and vecuronium bromide, Rocuronium bromide appears to be promising. Theoretically, it should have rapid onset of action as more number of molecules are available at neuromuscular junction to block receptors. At doses of 2 X ED95 (0.6 mg/kg), its onset of action ranges from 89±33 sec with duration of action 37±15 min and at doses of 3 X ED95 (0.9 mg/kg), 75±28 sec and 53±21 min[6].

Though higher dose reduce the onset time but it prolongs the duration of action which may not be acceptable. Some of the techniques which can shorten the onset time of neuromuscular block without using a higher dose of non-depolarising muscle relaxants are (1) priming technique[2] (2) timing principle[7] (3) manipulating the

cardiac output and muscle blood flow using drugs like ephedrine, phenylephrineetc[8].

Due to the chances of decreased airway protection and chances of aspiration, priming cannot be used as a technique to hasten the onset of action of Rocuronium in rapid tracheal intubations. Timing principle also has the same disadvantages. Hence the principle of manipulating the cardiac output using drugs like ephedrine appears to be a useful technique.

Ephedrine is claimed to be useful in reducing the onset time aftersuccinylcholine[9], pancuronium, vecuronium[10] and rocuronium[5]. It is also claimed to improve the intubating conditions after cisatracurium[10]. In addition, the use of ephedrine is supposed to reduce the onset time of rocuronium.

Studies suggest that pre-treatment with ephedrine may help to maintain the hypotension after induction agent like propofol. One study suggest that pre-treatment with ephedrine reduces the pain of propofol injection[11]. Hence the present study was undertaken to evaluate the effect of Pre-treatment with ephedrine 70 μg/kg on the intubating conditions and hemodynamic parameters 60 seconds after rocuronium at a dose of 0.6 mg/kg, which is the 2 X ED95 dose of the drug.

The dose of 70 μg/kg of ephedrine has been used in the studies done by Peter Szmuk et al[5], Munoz HR et al[4], Kim et al[10] and Tan et al[12] had used co administration of 15 mg ephedrine with propofol induction agent. However, a fixed dosage of ephedrine (not based on the patient's body weight) was used and their observations were not substantiated with neuromuscular monitoring. The authors suggested the need for further studies to identify the ideal dose of ephedrine along with quantitative measurement of the onset of neuromuscular block. Thus our study correlates with the above mentioned studies.

Komatsu et al in their study used ephedrine in the dose 210 μg/kg for pre-treatment. Kim et al evaluated three different doses of ephedrine 30, 70 and 110 μg/kg which were given 30 seconds before induction agent.

Gopalakrishna MD and others studied the effect of ephedrine 75, 100 and 150 μg/kg. We used an ephedrine dose of 70 μg/kg to minimize the risk of adverse effects, since 110 μg/kg of ephedrine is reported to be associated with marked hypertension and tachycardia after intubation, whereas 30 μg/kg of ephedrine was found not to improve the intubating conditions[8]. Hence the dose chosen in our study tallies with the studies of Peter Szmuk et al, Munoz HR et al and Kim et al.

Timing of ephedrine: In the present study ephedrine70 μg/kg was administered after pre-oxygenation (for 3 minutes), 1 min prior to the administration of induction agent. Rocuronium was administered 1 min after the induction agent and laryngoscopy was done after 60 sec. Hence ephedrine was given 2 min prior to Rocuronium bromide. This was done due to the peak effect of ephedrine on cardiac output and muscle blood flow occurs at 1-2 min. Most of the studies (Kim et al, Szmuk et al, Munoz et al) evaluated the effect of ephedrine 30 sec prior to induction agent. Han et al in their study evaluated the effect of timing of ephedrine administration (4 min vs 30 sec) on the assumption that the peak effect of ephedrine on cardiac output occurs at 4 min. However they found out in their study that the peak effect of ephedrine occurs at 1-2 min.

Gopalakrishna et al[3] have studied the effect of ephedrine given 1 min before induction agent on the effect of rocuronium. Our study method is comparable to the study done by Gopalakrishna et al.

Induction agent and dosage and opioids: In our study, Propofol 2.5 mg/kg rounded off to the nearest 0.5 mg is used as the induction agent. Out of the several induction agents available for rapid tracheal intubation, thiopentone, ketamine, etomidate and propofol have been evaluated by different authors in different studies.

Baraka et al[13] in their study compared thiopentone with ketamine as induction agents in caesarean section and found out that ketamine produced better intubating conditions.

Fuchs-Buder et al[14] observed that though there was no influence of induction agent (thiopentone or etomidate) on intubating conditions, the diaphragmatic movements were more attenuated with etomidate.

Skinner et al[15] in their study observed that propofol 2.5 mg/kg produced better intubating conditions with rocuronium as compared to etomidate 0.3 mg/kg. Choice of the induction agent for rapid sequence induction may play an important role in tracheal intubating conditions. Superior intubating conditions following propofol were attributed to greater suppression of upper airway reflexes, potentiation of rocuronium and non-equipotent anaesthetic doses. The presser response to intubation in propofol group was offset by its effect on systemic vascular resistance. Hence we chose2.5 mg/kg of propofol as induction agent in this study.

The choice of induction agent in this dosage concurs with the studies of Dobson et al, Skinner et al, Sparret al. and Gopalakrishna MD et al. Preservative free lidocaine (2%) 1 ml was added to every 10 ml of propofol to relieve the pain on injection as followed by Gopalakrishna et al. Thus our study is supported by their studies.

For further enhance the intubating conditions addition of opioids like alfentanil to the induction agent is shown by Sparr et al and Puhringer et al. Although as reported opioids have no influence on the neuromuscular blocking effects of rocuronium, they can improve the intubating conditions by reducing the stress response to intubation. Opioids were omitted in the present study as we were more interested on the effect of pre-treatment with ephedrine on the intubating conditions.

Neuromuscular monitoring: In the present study, neuromuscular Monitoring was not done to monitor the onset of neuromuscular block. This is because there are several reports to suggest that the measurement of onset of paralysis at adductor pollicis is not always reflective of ideal intubating conditions.

Meistelman et al[16] showed that, With a dose of 0.5 mg kg^{-1} of rocuronium, the onset time of paralysis at larynx is 1.4 ± 0.1 min compared to that at adductor pollicis 2.4±0.2 min. At this dosage, the maximum blockade achieved at adductor pollicis is 98±1% while it was 77±5% at the larynx.

Cantineau et al[17], using an intubating dose of 0.6 mg/kg of rocuronium observed that maximum neuromuscular blockade at adductor pollicis occurs at 80±20 sec while it was significantly longer for the diaphragm at 120 ±62 sec. Due to this poor correlation between neuromuscular monitoring and intubating conditions Dobson et al considered that it was more important to adhere to a rapid sequence protocol than delay tracheal intubation during the calibration period of a neuromuscular transmission monitor.

Our study is not supported by the above mentioned study as the neuromuscular monitoring was not used by us.

Tube size: In our study we used cuffed oral endotracheal tube (PORTEX®) of size 7.0 mm ID for female patients and 8.5 mm ID for male patients for intubation. Gopalakrishna MD et al had used cuffed endotracheal tubes of size 7 & 8 mm ID for adult female and male patients respectively.

Sparr et al had used cuffed endotracheal tubes of size 7.5 & 8.5 mm ID for adult female and male patients respectively. Hence our study is comparable to the above mentioned studies.

Scoring intubating conditions: In the present study we used the scoring system proposed by Cooper et al. to assess and score the intubating conditions based on the criteria for jaw relaxation, vocal cord position and intubating response. Each criterion was graded from 0-3 as shown in the following table.

Scoring of intubating conditions

Score	Jaw relaxation (ease of 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	Diaphragmatic movements
3	Good (easy)	Open	None

The intubating conditions were graded as excellent (score 8-9), good (score 6-7), fair (score 3-5) and poor (score 0-2). Excellent and good conditions were considered clinically acceptable, while fair or poor conditions were considered clinically unacceptable.

In different studies by Skinner et al, Han et al, Tan et al, and Kim et al, used the same scoring system as we used in this study. However in a study by Gopalakrishna MD et al. used the scoring system as per the intubation scoring system of the Consensus Conference on Good Clinical Research Practice in Pharmacodynamic Studies of Neuromuscular Blocking Agents, Copenhagen consensus. This scoring system is not used in any other study.

In a study Jeffrey Joseph Perry et al[10] used a different scoring system proposed by Goldberg et al in their meta-analysis and converted the results of studies using different scoring systems to Goldberg system for their analysis.

In our study, jaw relaxation (ease of laryngoscopy) was considered to be easy in 49 (98%) and fair in 1 (2%) patients in the ephedrine pretreated group whereas jaw relaxation (ease of laryngoscopy) was considered to be easy in 46 (92%), fair in 3 (6%) and difficult in 1 (2%) patients in the normal saline group.

In the ephedrine pretreated group, vocal cords were open in 45/50 patients (90%) while in the normal saline group (n=50) the vocal cords were assessed to be open in 43 (86%), moving in 4 (8%), closing in 2 (4%) and closed in 1 (2%) patient.

During laryngoscopy, in the ephedrine pre-treated patients, 26 (52%) had no diaphragmatic movements. 16 (32%) slight diaphragmatic movements, 7 (14%) mild coughing and 1 (2%) severe coughing or bucking. In the saline pretreated group, 20 (40%) patients had no response, 13 (26%) slight diaphragmatic movements, 10 (20%) mild coughing and 7 (14%) severe coughing or bucking (p=0.110)

With regard to assessment of overall intubation conditions, in the ephedrine pre- treated group 42 (84%) had excellent (intubation score 8-9) and 8 (16%) patients had good (intubation score 6-7) intubating conditions. However in the saline pretreated group, 32 (64%) patients had excellent intubating conditions, 13 (26%) patients had good intubating conditions and 5 (10%) patients are assessed to have fair (intubation score 3-5) intubating conditions. Based on this scoring system, clinically acceptable intubating conditions at 60 secs after rocuronium were present in 100% of patients in the ephedrine pretreated group. However in the normal saline group, clinically acceptable intubating conditions at 60 sec after rocuronium were present in 90% of patients and unacceptable in intubating conditions were present in 10% of patients. Statistically significant

difference (p=0.023) was found between ephedrine pre-treated group and saline pretreated group suggesting better intubating conditions in the ephedrine pretreated group.

In their study Tan et al[12] found that clinically acceptable intubating conditions were present in all patients belonging to ephedrine propofol group as well as propofol group. However, the proportion of excellent intubating conditions was significantly higher in the propofol ephedrine group (84%) than in the propofol group (32%). Vocal cord position and diaphragmatic response to intubation was significantly less in the propofol ephedrine group than in the propofol group. This study was done using a fixed dose of ephedrine 15 mg added to propofol 2.5 mg/kg given before rocuronium 0.6 mg/kg and did not base the dosage on patient's body weight.

Gopalakrishna MD et al[3] in their study found that 75 µg/kg of ephedrine given before tracheal intubation with propofol 2.5 mg/kg and rocuronium bromide 0.6 mg/kg resulted in clinically acceptable intubating conditions in24/25 patients (intubation score, excellent 15; good 9) while in the control group clinically acceptable intubating conditions were found in 19/25 patients. The intubation score was excellent in only 4/25 and good in 15/25 patients. The intubating conditions were judged to be poor in 6/25 patients in the control group. The results were found to be statistically highly significant (p=0.003)

Han et al[18] in their study found that pretreatment with ephedrine either4 min earlier to rocuronium or 30 secs earlier to rocuronium produced clinically acceptable intubating conditions in 100% of patients, similar to the control group. However excellent intubating conditions were present in 24/25 patients with ephedrine administered 4 min prior to rocuronium, in 22/25 patients with ephedrine administered 30 secs prior to rocuronium and in 21/25 patients in the control group. This statistically insignificant difference can be attributed to the performance of intubation within 20 sec of the time of maximum depression of the electromyographic response in all the patients. It is significant to note that this time was achieved within 64 sec in patients with ephedrine administered 4 min prior to rocuronium, within 72 sec in patients with ephedrine administered 30 sec prior to rocuronium, while in the control group this was achieved at 80 sec. The results obtained in our study are hence comparable to those obtained by Tan et al, Gopalakrishna MD et al and Han et al.

In our study, the time for intubation (number of seconds from the first contact of the intubator to successful placement of endotracheal tube) and duration of laryngoscopy (time from insertion of the laryngoscope blade into the patient's mouth to its removal after successful intubation) were recorded in all the patients in both the groups. In the ephedrine pretreated group the duration of laryngoscopy was 11.48±2.915 secs and in the control group it was 11.5±3.558sec.

In the ephedrine pre-treated group the time taken for intubation was 18.2±3.083 sec and in the control group it was 19.5±6.914sec. The mean duration of the time taken for laryngoscopy and intubation time were comparable in both the groups (p = 0.975 and 0.227) respectively.

In their study Gopalakrishna MD et al found that the duration of laryngoscopy was 14 secs (14±5) in the propofol ephedrine group while it was13±4 secs in the control group, which was statistically not significant.

Haemodynamics

In the present study, the basal mean heart rates in both the groups (group EPR and group SPR) were comparable. (86.44 vs 89.0 bpm). There was a statistically significant increase in mean heart rate in the Ephedrine Propofol Rocuronium group after administration of ephedrine (90.46 bpm) which was not observed in the Saline Propofol Rocuronium group (86.28 bpm). The heart rate fell marginally to 85.68 bpm after administration of propofol in the Ephedrine Propofol Rocuronium group and to 80.74 bpm in the control group, which was statistically significant. Similar significant decreases were observed between the two groups during administration of rocuronium 1 min after propofol. However the heart rate rose 1 min after tracheal intubation to statistically significant levels.

The post intubation tachycardia persisted in both the groups till the end of the study group which was statistically not significant.

In our study the basal systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressures (MAP) were comparable in both the groups. In the Ephedrine Propofol Rocuronium group, compared to the baseline systolic blood pressure, there was statistically significant increase in systolic blood pressure after ephedrine administration. Systolic blood pressure fell significantly after propofol and there was an increase during intubation and 1 min after intubation which was statistically significant. In the SPR group compared to baseline systolic blood pressure, there was a statistically significant fall in systolic blood pressure for 2 minutes after propofol administration. Systolic blood pressure rose to statistically significant levels during and1 min after intubation. Comparison between the two groups showed that the increase in systolic blood pressure after administration of ephedrine, and the reduction in systolic blood pressure during and 1 min after administration of propofol and the later increase in systolic blood pressure 1 min post intubation were statistically significant.

Statistical evaluation between the groups showed a statistically not significant fall in diastolic blood pressure in group Saline Propofol Rocuronium after propofol administration, and an increase at intubation and 1 min after intubation. The mean diastolic blood pressure increase observed at intubation 1 min and 2 min after

intubation in group Ephedrine Propofol Rocuronium was statistically significant compared to mean diastolic blood pressure in group Saline Propofol Rocuronium($p<0.05$).

In the Ephedrine Propofol Rocuronium group, there was a statistically significant change in mean arterial pressure during the 1st 2 minutes after ephedrine administration and at the 4th min (during tracheal intubation) when compared to the baseline. In the Saline Propofol Rocuronium group, similar statistically significant deviations from the baseline in mean arterial pressure were observed during the 1st 2 minutes after propofol administration and this continued till the 2nd min post intubation. Between the two groups there was a statistically significant difference in mean arterial pressure during intubation (89.48 mm Hg (Ephedrine Propofol Rocuronium) vs 107.72 mm Hg (Saline Propofol Rocuronium) and 1 min later (93.94 mm Hg (Ephedrine Propofol Rocuronium) vs 102.18 mm Hg (Saline Propofol Rocuronium).

Considering that in the present study methods, any deviation from the baseline of more than 30% to be considered as clinically significant, these variations in systolic, diastolic and mean blood pressures were clinically not significant and hence comparable.

In their study, Tan et al, who had used a fixed dose of ephedrine 15 mg added to propofol 2.5 mg/kg, found that there was significant increase in the heart rate and mean arterial pressure in the propofol ephedrine group ($p<0.0001$:$p<0.0015$) respectively. Two patients in the propofol-ephedrine group and one patient in the propofol group developed occasional single ventricular ectopic beats during intubation that reverted back to normal within a few seconds.

In their study, Han DW et al (2008) who evaluated the significance of injection timing (4 min vs 30 secs) of ephedrine 70 μg/kg prior to rocuronium0.6 mg/kg observed that heart rate increased immediately after tracheal intubation and at 1 min and 2 min after tracheal intubation in both the groups which was statistically highly significant ($p=0.013$, $p<0.001$) respectively, while in the control group, tachycardia was seen at 1 min after intubation. They observed that mean arterial pressure was significantly increased in patients receiving ephedrine30 secs prior to rocuronium group immediately after tracheal intubation ($p=0.009$) while it was significantly decreased in the control group just before intubation ($p<0.001$) and 2 min after intubation ($p=0.001$).

Gopalkrishna MD et al observed that there was a statistically significant increase in the heart rate in groups which 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 a statistically significant difference in mean arterial pressure between groups which received 75 and 150 μg/kg of ephedrine. However in their study, considering 20% deviation from the baseline as clinically significant, all the groups were comparable during the first 5 minutes after intubation.[7]

Our finding that the mean arterial pressure fell in the immediate post induction period, despite pretreatment with ephedrine is similar to that observed by Gopalakrishna MD et al. This is in accordance with their observation that prophylactic injection of ephedrine only attenuates, but does not completely abolish the decrease in arterial pressure associated with induction of anaesthesia.

The findings of the present study that pretreatment with low dose ephedrine produces tachycardia and does not cause clinically significant blood pressure changes are similar to those of Tan et al, Gopalakrishna MD et al and Han et al.

Hence our study is supported by the views of Tan et al, Gopalakrishna MD et al and Han et al that caution needs to be exercised in the subset of patients in whom ephedrine induced tachycardia might be detrimental (e.g. patients with ischemic heart disease). In such cases, the risk of tachycardia has to be weighed carefully against the benefit of improved intubating conditions.

Side effects and adverse events, if any: No major side effects, attributable to the study drugs were observed during this study. One patient in the Ephedrine Propofol Saline group (patient No 27) had unanticipated difficult airway. Though the intubation score was good (6), she could not be intubated with No 7 mm ID endotracheal tube. Intubation was possible only at the3rd attempt with the stylet and No 6.5 mm ID endotracheal tube but there was no desaturation and her peri-operative and post-operative course was uneventful.

Limitations

1. Subjective scoring: Though the observer was blinded to the study drug, the scoring system for intubation is highly subjective. Hence assignment of different scores to their criteria may be subject to variation.
2. Duration not included: Our study design did not include the effect of ephedrine on the duration of action of rocuronium. Hence in both the groups duration of action, which may be relevant in rapid sequence induction, was not measured.
3. Cardiac output was not measured: In the present study, cardiac output was not measured and hence the effect of ephedrine on cardiac output cannot be confirmed.

Conclusion

From the results of our study we conclude that:

1. Pre-treatment with Ephedrine hydrochloride 70 μg/kg provides better intubating conditions compared to propofol 2.5 mg/kg alone during rapid tracheal intubation 60 seconds after 0.6 mg/kg rocuronium bromide injection.
2. Pre-treatment with Ephedrine hydrochloride 70 μg/kg prior to induction with propofol 2.5 mg/kg and rocuronium bromide 0.6 mg/kg does not have

any effect on the duration of laryngoscopy and time taken for intubation.

3. Pre-treatment with Ephedrine hydrochloride 70 µg/kg resulted in statistically significant increase in the heart rate compared to the control group 1 min post intubation. However it did not produce clinically significant elevations of systolic blood pressure, diastolic blood pressure and mean arterial pressure from the baseline.

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