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## Original Research Article

## Evaluation of single dose ephedrine on the onset time of rocuronium bromide- A prospective randomized double blind study

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## ABSTRACT

**Background:** Ephedrine, an  $\alpha$ 1 and  $\beta$  agonist, that increases blood flow to muscles and thus increases the cardiac output. This concept is used in this study as speed by which the drug reaches the neuromuscular junction partly determines the onset of action of muscle relaxants. Our hypothesis was that ephedrine could hasten the onset of action of rocuronium bromide. The onset time of rocuronium was shorter after administration of ephedrine and there was no difference in the laryngoscopic views and hemodynamics between the two groups.

**Aim:** Evaluation of the effects of a single dose of ephedrine on the onset time of rocuronium bromide and hemodynamic parameters during induction sequence and on the laryngoscopic views.

**Settings and Design:** Prospective randomized double blinded study.

**Materials and Methods:** 50 patients of the age 18 years or above belonging to ASA I or II posted for elective ENT surgeries under general anaesthesia were randomly allocated into two groups, namely Group E (ephedrine) and Group S (saline) by computer generated random allocation.

**Statistical Analysis:** Onset time of rocuronium, POGO score and hemodynamics were analyzed using student's t-test and the results are shown as mean and standard deviation.

**Results:** The onset time of neuromuscular blockade for tracheal intubation was significantly shorter in ephedrine group. Hemodynamic parameters were comparable in both groups, so were the laryngoscopic views.

**Conclusion:** Pre induction ephedrine administration dose of 70 mcg/kg hastens the onset of action of rocuronium bromide with minimal hemodynamic changes.

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## 1. Introduction

The risk of patient going into hypoxia and pulmonary aspiration is high during the period from induction to tracheal intubation. Endotracheal intubation is frequently facilitated by administration of muscle relaxants of shorter onset which helps in reducing the duration of this period. Suxamethonium may be associated with side effects such as prolonged paralysis, postoperative myalgia, increased intraocular, intracranial

and intraabdominal pressures and hyperkalemia.<sup>1-3</sup> Hence the best alternative to suxamethonium among the non-depolarizing neuromuscular blocking agents is rocuronium for rapid tracheal intubation. Larger doses of rocuronium is inevitably associated with prolonged duration of action, therefore to achieve optimum intubation condition with lower dose of rocuronium, ephedrine is used to reduce the onset time of rocuronium.<sup>4-6</sup> The onset of action of neuromuscular blockers are primarily dependent on the cardiac output and blood flow to the muscle groups. Since ephedrine can increase these variables,<sup>7,8</sup> it can thereby reduce the onset of action of muscle relaxants. The aim of

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this study was to evaluate the effects of a single dose of ephedrine given just before the induction on the onset time of rocuronium and to record the change in hemodynamic parameters during the induction sequence and on the laryngoscopic views.

## 2. Materials and Methods

After obtaining institutional ethical committee clearance and written informed consent, 50 patients of age  $\geq 18$  years and above with ASA grade I or II posted for elective ENT surgeries under general anaesthesia were enrolled for the study and randomly allocated into two groups viz Group E (ephedrine) and Group S (saline) by computer generated random allocation. Patients with difficult airway, active or long standing respiratory issues, pregnancy, history of GERD, severe cardiovascular disease, musculoskeletal abnormality affecting cervical vertebrae, history of anaphylactic reaction to the anaesthetic drugs were excluded from the study.

All patients underwent a comprehensive pre anaesthetic assessment the day before surgery that included a thorough physical examination and investigations. They were fasted overnight, and were given 150 mg of ranitidine and 10 mg of metoclopramide for acid aspiration prophylaxis 1 hour prior to surgery. In the operation theatre, five lead electrocardiogram, oxygen saturation (SpO<sub>2</sub>), non-invasive blood pressure, neuromuscular monitoring (TOF) were connected. The patients were premedicated with fentanyl 2 mcg/kg given intravenously 5 minutes prior to induction. The patients were preoxygenated with 100% oxygen for 3 minutes. Baseline cardio-respiratory parameters like blood pressure, heart rate, SpO<sub>2</sub> were recorded before induction. Both the patient and the anaesthetist administering general anaesthesia was blinded to the study drug. Patients were given either ephedrine 70 mcg/kg or equal volume of saline 1 minute prior to induction which was indicated by the investigator to the anaesthetist. Patients were induced with 2 mg/kg of propofol intravenously and neuromuscular blockade was achieved with rocuronium 0.6 mg/kg. All patients were monitored at ulnar nerve for supramaximal stimulus of 15% above maximal stimulus with TOF after induction with propofol but before administration of rocuronium. Outcomes measured were onset time of rocuronium, POGO (percentage of glottic opening) score and hemodynamics. Onset time of rocuronium was defined as the time from the end of injection of rocuronium to disappearance of all four twitches of train of four in neuromuscular monitoring. Heart rate and Blood pressure were measured pre-operatively, induction, during test drug administration and 1, 3 min after intubation. Laryngoscopic view was assessed using POGO score.

### 2.1. Statistical analysis

Statistical analysis was done using SPSS version 15.0. Outcome measures (onset time of rocuronium, POGO score and hemodynamics) were analyzed using student's t-test and the results are shown as mean and standard deviation. Statistical significance was considered when P value  $< 0.05$ . The required sample size was calculated using openepi.com from a previous similar study and a sample size of 25 in each group was enough to detect a difference of 25% ( $p_1 = 25\%$  and  $p_2 = 60\%$ ) keeping alpha error at 5% and power of the test as 80%.

## 3. Results

**Table 1:** Demographic data

	<b>Group E (ephedrine)</b>	<b>Group S (saline)</b>
<b>Age (years)</b>	31 $\pm$ 12.43	31.4 $\pm$ 11.48
<b>Weight (Kg)</b>	58 $\pm$ 9.63	55.12 $\pm$ 8.96
<b>Height (cm)</b>	153.5 $\pm$ 6.08	155.75 $\pm$ 5.99
<b>Sex</b>		
Male	12	13
Female	13	12

Values expressed as mean  $\pm$  SD.

Both the groups were comparable in terms of demographic data (Table 1).

**Table 2:** Outcome measures

	<b>Group E (ephedrine)</b>	<b>Group S (saline)</b>
<b>Onset time of Rocuronium (seconds)</b>	44.80 $\pm$ 15.76	57.88 $\pm$ 17.53*
<b>POGO score (%)</b>	80.20 $\pm$ 15.67	74.40 $\pm$ 26.94

\*p value  $< 0.05$ , Values expressed as mean  $\pm$  SD.

The onset time of neuromuscular blockade for tracheal intubation as detected by TOF was significantly ( $p = 0.003$ ) shorter in ephedrine group (44.80  $\pm$  15.76 seconds) than the saline group (57.88  $\pm$  17.53 seconds) shown in Table 2.

Trachea was successfully intubated in patients with clinically acceptable intubating conditions at the first attempt in all the patients. POGO scoring (80.20  $\pm$  15.67 vs 74.40  $\pm$  26.94) was comparable in both the groups. The baseline values of heart rate, systolic and diastolic blood pressure were similar in both the groups. Data of Heart rate and blood pressures as shown in Table 3 showed that the patients in both the groups were comparable.

## 4. Discussion

Succinylcholine is a well established drug for rapid sequence induction but in conditions where its use is contraindicated like burns, hyperkalemia, raised intracranial

**Table 3:** Hemodynamics

	<b>Group E (ephedrine)</b>	<b>Group S (saline)</b>
<b>Heart rate (rate/min)</b>		
Baseline	91.08 ±15.87	93.08 ±18.62
Induction	104.48 ±13.38	100.24 ±18.80
During test drug	98.52 ±17.37	95.32 ±18.62
1 min after intubation	114.04 ±15.39	105.92 ±19.40
3 min after intubation	108.40 ±13.72	101.96 ± 17.01
<b>Systolic blood pressure</b>		
Baseline	128.33 ±13.05	131.88 ±15.43
Induction	116.36 ±16.77	120.28 ±13.10
During test drug	130.80 ±16.23	125.56 ±15.72
1 min after intubation	129.92 ±20.33	135.44 ±28.96
3 min after intubation	127.68 ±17.74	125.27 ±16.38
<b>Diastolic blood pressure</b>		
Baseline	81.88 ±7.24	87.28 ±7.92
Induction	80.72 ±13.23	76.72 ±13.09
During test drug	81.48 ±10.08	83.40 ±8.04
1 min after intubation	87.24 ±13.94	92.24 ±19.32
3 min after intubation	78.96 ±13.00	85.12 ±10.54

\*p value < 0.05, Values expressed as mean ± SD

pressure, malignant hyperthermia etc, rocuronium has been a suitable alternative in doses ranging from 0.9 – 1.2 mg/kg. This is predominantly due to its fast onset of action and our results further substantiated the former evidence that ephedrine accelerates the onset time of rocuronium bromide. The mechanism of action could be due to the increased cardiac output and muscle vasodilatation caused by ephedrine which in turn reduces the circulation time of rocuronium.<sup>8</sup> Munoz et al studied that the co administration of ephedrine 70 mcg/kg shortens the onset time of rocuronium by 26% which was similar to the results (44.80 ± 15.76 vs 57.88 ±17.53 seconds) of our study. The difference was that they compared ephedrine with esmolol and we compared ephedrine with saline (placebo).<sup>9</sup> Ezri and colleagues studied the manipulation of cardiac output by pretreatment with ephedrine or Esmolol. They estimated the cardiac output by NICO (noninvasive cardiac output) method and found that ephedrine or esmolol affects the onset time of rocuronium bromide and in their study, they administered the same dose of ephedrine administered in our study and they had a shorter onset time of 52.2±16.5 seconds.<sup>10</sup> Another study compared the intubating conditions after induction with propofol alone vs propofol-ephedrine which was followed by rocuronium in 100 patients and found out that there was significant improvement in intubating conditions in propofol-ephedrine group with hemodynamic stability.<sup>11</sup>

Another study compared the effects of different doses of ephedrine on providing intubating conditions and hemodynamics during rapid tracheal intubation, they found ephedrine when given at 75 or 100 mcg/kg, and induction done with propofol and rocuronium, it improved the intubating conditions.<sup>12</sup> They hypothesized that by increasing cardiac output and increasing perfusion to laryngeal and diaphragmatic muscles,<sup>13</sup> it improved the intubating conditions but we found no difference in the intubating conditions with rocuronium and ephedrine in our study.

Although we expected hemodynamic changes in our study, we didn't encounter any patient with tachycardia, hypertension or cardiac arrhythmias during the administration of ephedrine which was very similar to the results of previous studies. Munoz and colleagues studied the effect of ephedrine on the onset time of rocuronium and found that there was no significant hemodynamic instability in their study. Ephedrine was used in the similar dose as our study but the induction agent they used was thiopentone 4 mg/kg.<sup>9</sup> Smith and colleagues studied the intubating conditions and onset of action of vecuronium 0.1 mg/kg and rocuronium 0.6 mg/kg in a randomized controlled trial and found that the intubating conditions were better with rocuronium and there was hemodynamic stability in both the groups which was very similar to our results.<sup>14</sup> There was no incidence of any other adverse effects like anaphylactic reactions, cardiac arrhythmias, rashes, bronchospasm etc. in our study.

## 5. Conclusion

Pre induction ephedrine administration dose of 70 mcg/kg hastens the onset of action of rocuronium bromide with minimal hemodynamic changes.

## 6. Source of Funding

None.

## Conflicts of Interest

The authors declare no conflict of interest.

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