

## Quality of Laryngoscopic View and Rapidity of Development of Intubating Conditions after Atracurium, Vecuronium and Rocuronium: A Randomized Controlled Study

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### Abstract

**Introduction:** The choice of muscle relaxant for endotracheal intubation may be straightforward in selective cases, but in most patients, who are otherwise uncomplicated, poses a dilemma among anesthesiologists and intensivists. The authors examined the most commonly used muscle relaxants (Vecuronium, atracurium and rocuronium) in equipotent doses and compared the most vital parameters, i.e., rapidity of development of clinically acceptable intubating condition and quality of laryngoscopic view.

**Method:** 150 adult patients of 18 to 50 y of age were recruited randomly into 3 equal groups having 50 patients (n=50) in each and equipotent dose of vecuronium, atracurium and rocuronium was administered. Endotracheal intubations were attempted every 30 seconds till excellent or good intubating conditions were achieved upto a maximum of 240 s. The available data were analyzed statistically.

**Results:** The three study groups were comparable in terms of the demographic characteristics. The quality of intubating condition was rated significantly better with Rocuronium than with Vecuronium and Atracurium. Time required to achieve successful intubation was also significantly less with rocuronium than with Vecuronium ( $107.48 \pm 1.98*6.583$  s vs.  $165.46 \pm 1.98*6.790$  s) and Atracurium ( $107.48 \pm 1.98*6.583$  s vs.  $195.43 \pm 1.98*6.583$  s). Excellent laryngoscopic condition was found in more patients with rocuronium at 60 and 90 s and number of successful intubation was also higher.

**Conclusion:** Therefore, the study confirms that rocuronium produces clinically acceptable intubating condition earlier than the other two drugs and the quality of intubating condition is better in terms of laryngoscopic view.

**Keywords:** Muscle relaxants; Laryngoscopy; Intubating conditions; Rocuronium; Atracurium; Vecuronium

### Introduction

From time immemorial the quest for an ideal anesthetic agent considered as the ultimate goal in anesthesia research. Scientists and chemists experimented over innumerable drugs and chemicals to find an agent which can provide sedation, analgesia, amnesia, muscle relaxation and loss of reflex response without any hemodynamic instability or undue adverse effect but failed to establish a single drug as a sole remedy of surgical stress. Modern anesthesia practice involves use of multiple drugs, e.g., sedatives, neuromuscular blockers (NMBs), analgesics etc., to achieve and maintain adequate plane of anesthesia during surgery. Among NMBs currently three agents very commonly used in the anesthesia practice, namely: atracurium, vecuronium and rocuronium. All these three drugs are intermediate acting non-depolarising neuromuscular blockers with unique advantages and disadvantages which guides their use in selective cases (Like atracurium or cisatracurium in renal or hepatic insufficiency owing to its liver or kidney independent unique metabolism: Hofmann elimination and nonspecific ester hydrolysis) [1-5]. But for general purpose, the ideal and best neuromuscular blocker is still to be investigated. For surgery under general anesthesia, maximum muscle relaxation is required during laryngoscopy and intubation. Therefore the neuromuscular blockers are usually judged in terms of their ability to produce ideal intubating conditions as well as quality of muscle relaxation after a specified time period.

In this background, the aims of this study were aimed to evaluate the quality and speed of development of clinically acceptable tracheal

intubating conditions after administration of equipotent doses of Vecuronium, Atracurium and Rocuronium and to compare the timing of achievement of successful intubation in adults after administration of equipotent doses of the three drugs.

### Patients and Methods

After obtaining research approval from Institutional research oversight committee and informed written consent from the patients, this randomized double blind study was conducted on 150 patients between 18 to 50 y of age (Table 1), ASA physical status I and II posted for surgery under general anesthesia. Patients with anticipated difficult intubation, refused consent, contraindication to any drug under study (e.g., hepatic or renal insufficiency), any neuromuscular disorder, dyselectrolytemia, pregnancy or patients receiving drugs influencing neuromuscular transmission were sorted out in preoperative clinic and excluded. Patients were recruited to three groups according to

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Drugs	ED 95	Doses considered for intubation, i.e., 2 X ED95
Vecuronium [7-12]	0.05 mg/kg	0.1 mg/kg
Atracurium [12-15]	0.23 mg/kg	0.25 mg/kg
Rocuronium [7,16-20]	0.3 mg/kg	0.6 mg/kg

**Table 1:** Neuromuscular blockers: ED 95 values [6].

a computer generated randomization chart. Each group included 50 patients. Group A received 0.1 mg/kg vecuronium, group B received 0.5 mg/kg Atracurium and group C received 0.6 mg/kg rocuronium intravenous bolus as equipotent intubating dose of neuromuscular blocker.

After the patient was received in operating room, documents were checked, a brief examination was done and monitors were attached. Before intubation, ECG, pulse oxymetry, non-invasive blood pressure was monitored and after intubation end tidal carbon dioxide was also monitored. All patients were preoxygenated for 5 min and received glycopyrrolate (0.2 mg), fentanyl (2 µg/kg), ondansetron (4 mg) 5 min before induction. Propofol (2 mg/kg) was used as induction agent. After the patient was induced, equipotent dose of neuromuscular blocker was introduced to the patients according to their randomization group as described earlier

The time of administration of neuromuscular blockers were noted. Endotracheal intubations were attempted by experienced anesthesiologist using cuffed polyvinylchloride endotracheal tubes [sizes appropriate for the age and the body structure]. The first intubation attempt was made at 60 s, after administration of relaxant. Intubation conditions were scored as excellent, good or poor based on laryngoscopy [jaw relaxation], vocal cords position and movements and movement of limbs and coughing in response to intubation and/or cuff inflation using the scoring systems proposed by Viby-Mogensen [21] (Tables 2 and 3). Least achieved score in any of the variables would determine the score of tracheal intubating conditions.

Endotracheal intubation was not performed until intubating conditions had been assessed to be excellent at the end of 60 s or 90 s and excellent or good at the end of 120 s. Subsequent attempts were done at 30 seconds interval at 90 s, 120 s and the last attempt was made at 240 s until the intubation could be achieved with acceptable ease and the time of successful intubation was noted. Patients who did not achieve acceptable intubating conditions even at 240 s were managed with additional boluses of muscle relaxant and number of such patients were also noted. The study ended after successful intubation was achieved.

A difficult airway cart with instruments and devices for management of difficult airway was kept ready to combat emergency situation. The neuromuscular blockers were prepared by an anesthesiologist not involved in patient management and marked as 'Relaxant'. Intubation was done by an anesthesiologist unaware of the relaxant used. Data collection and analysis was performed by another anesthesiologist unaware of the group distribution.

For sample size calculation number of successful intubation at the end of 90 s was considered as the primary outcome measure. A pilot study was undertaken with 20 patients in each group and mean and standard deviation was measured. It was estimated that 45 subjects would be required per group in order to detect a difference of 10 patients with 80% power and 5% probability of type I error. Data was summarized as mean and standard deviation for parametric numerical variables and median and interquartile range for nonparametric numerical variables.

Variables	Excellent	Good	Poor
<b>Laryngoscopy (Jaw relaxation)</b>	Easy (Fully relaxed)	Fair (Not fully relaxed)	Difficult (Resistance)
<b>Vocal cord position</b>	Abducted	Intermediate	Closed
<b>Vocal cord movement</b>	None	Moving	Closing
<b>Reaction to intubation AND/OR Cuff Inflation</b>	None	Slight	Vigorous
<b>Movements of limbs/ Coughing</b>	None	Diaphragm*	Sustained

\*diaphragm indicates slight diaphragmatic movements only

**Table 2:** Endotracheal intubating condition score [21].

Airway Examination Component	Anticipated difficult intubation
<b>Length of upper incisors</b>	Relatively long
<b>Relationship of maxillary and mandibular incisors during normal jaw closure</b>	Prominent "overbite" (maxillary incisors anterior to mandibular incisors)
<b>Relationship of maxillary and mandibular incisors during voluntary protrusion of mandible</b>	Patient cannot bring mandibular incisors anterior to (in front of) maxillary incisors
<b>Interincisor distance</b>	Less than 3 cm
<b>Visibility of uvula</b>	Not visible when tongue is protruded with patient in sitting position (e.g., Mallampati class>2)
<b>Shape of palate</b>	Highly arched or very narrow
<b>Compliance of mandibular space</b>	Stiff, indurated, occupied by mass, or non-resilient
<b>Thyromental distance</b>	Less than three ordinary finger breadths
<b>Length of neck</b>	Short
<b>Thickness of neck</b>	Thick
<b>Range of motion of head and neck</b>	Patient cannot touch tip of chin to chest or cannot extend neck

Guided by Practice Guidelines for Management of the Difficult Airway; An Updated Report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway [22]

**Table 3:** Anticipated difficult airway.

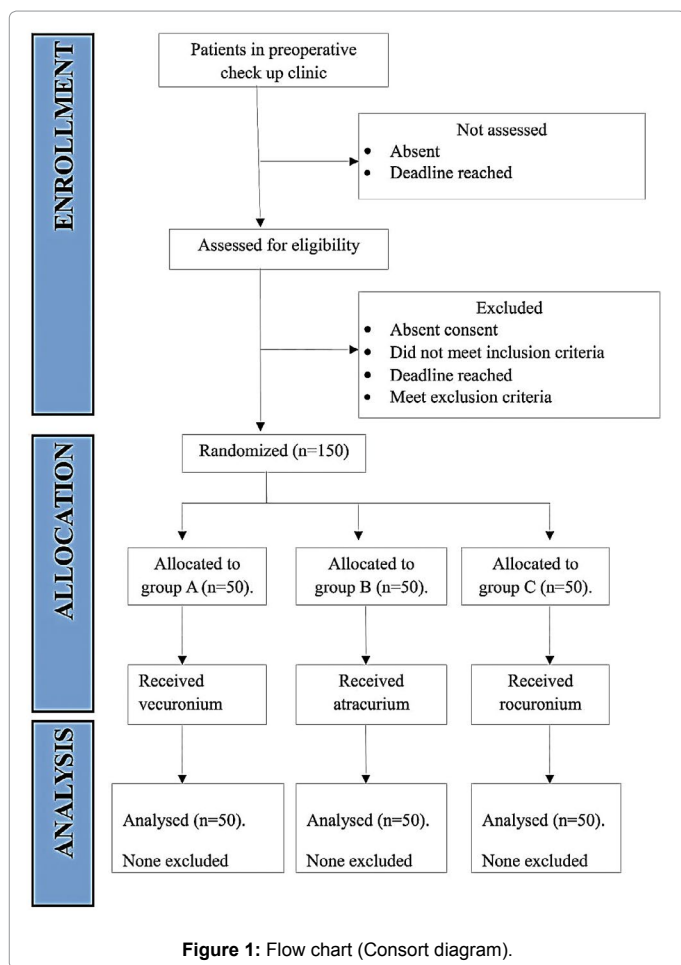
Counts and percentages were used for categorical variables. Parametric and nonparametric distribution was differentiated by Kolmogorov-Smirnoff Goodness of fit test. Numerical variables between groups compared by One-Way ANOVA. Categorical variables were compared by Chi-square test for post hoc comparison Tukey's test was applied (Figure 1).

## Results and Analysis

150 patients were enrolled for the study and randomized to three groups of 50 patients each (n=50). Group A received 0.1 mg/kg of Vecuronium, group B (n=50), received 0.5 mg/kg of Atracurium and group C (n=50), received 0.6 mg/kg of Rocuronium as intubating dose. Demographic variables, namely age, body weight and gender distribution compared between the groups and revealed no significant differences (p value 0.585, 0.092 and 0.861 respectively) (Table 4).

The time required for successful intubation was compared between the groups and revealed mean intubation time in Group C (107.48 ± 1.98 s) was significantly lower than in A (165.46 ± 1.98 s) and group B (195.43 sec ± 1.98 s) [One-Way ANOVA test for numerical values; p<0.001] [Mean ± Standard deviation]. When the intubation times between two individual groups were compared by Tukey's test for post-hoc comparison, the data showed that the intubation times in Group C was significantly different from those in Group A and Group B [p<0.001] (Figure 2).

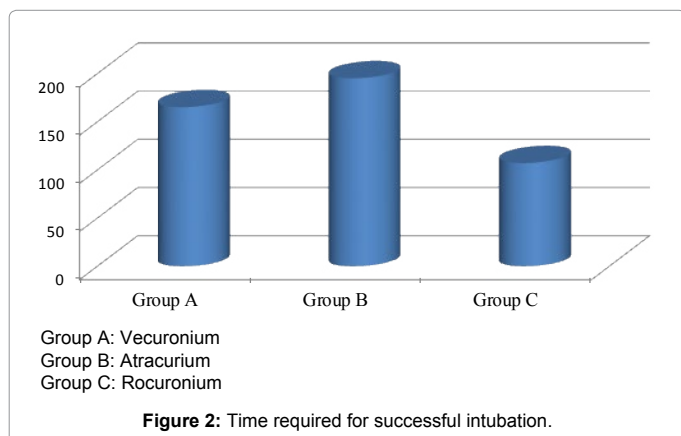
Numbers of successful intubation at 60 s, 90 s and 120 s were



	Group A (n=50) [Vecuronium]	Group B (n=50) [Atracurium]	Group C (n=50) [Rocuronium]	P value
Age (Years)	31.12 ± 6.08	29.89 ± 5.84	30.14 ± 6.62	0.585 <sup>A</sup>
Body weight (Kg)	54.16 ± 11.32	49.62 ± 9.35	51.16 ± 10.24	0.092 <sup>A</sup>
Gender [M/F (%)]	35/15 (70%/30%)	36/12 (74.47%/25.53%)	37/13 (74%/26%)	0.861 <sup>B</sup>

A. One way ANOVA (Significant if p value<0.05)  
 B. Chi-Square test 2 sided (Significant if p value<0.05)

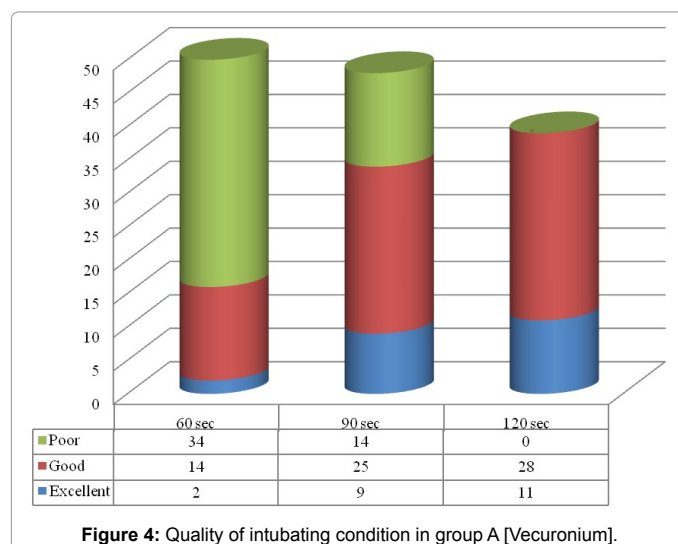
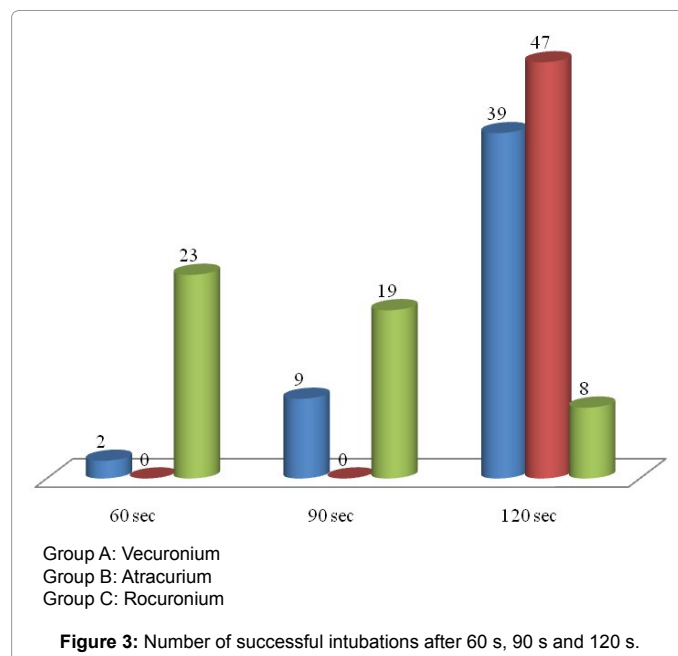
**Table 4: Demography.**



compared between the groups by Chi square test and significant differences were found between the groups. Individual groups, when compared with each other, it revealed Group C was significantly different from Group A and B [2-sided p value<0.001] and Group A and Group B are also significantly different [2-sided p value=0.002]. Number of successful intubation is more in group C after 60 and 90 s than other two groups (Figure 3).

The quality of intubating condition was compared between the groups after 1 min at 30 s interval up to 2 min and categorized as excellent, good and poor. In group A, excellent intubating conditions were developed in 22 patients. All other patients in group A developed good intubating conditions by 120 s. Most of the patients developed poor intubating conditions at the end of 1 min. The quality was mostly poor after 1 min and good after 60 and 90 s (Figure 4).

In group B, excellent intubating conditions were developed only in 16 patients after intubating dose and all of them developed excellent



intubating condition after 120 s. Intubating condition was mostly poor after 60 s. Three patients did not develop good intubating conditions even after 240 s and required additional anesthetics and neuromuscular blocker (Figure 5).

Whereas in group C excellent intubating condition obtained in 50 patients and of which 23 were reached within 60 s (Figure 6).

## Discussion

The most accurate assessment of potency of a neuromuscular blocking drug is aided by its ability to depress twitch height [5-17]. The drug dose relationship is established by calculating the required dose of neuromuscular blocking agent to produce a certain response. The dose required to produce 50%, 90%, or 95% depression of twitch height is commonly expressed as ED50, ED90, and ED95 of a drug and it is considered as a measurement of potency. Therefore to compare between neuromuscular blockers one must use the dose which is same multiplier of ED50 or ED95 [6,7,20,23-33]. In this study, the authors used twice the ED 95 dose for intubation in all three groups. The ED 95 values of the three muscle relaxants with intubating dose is depicted in Table 1.

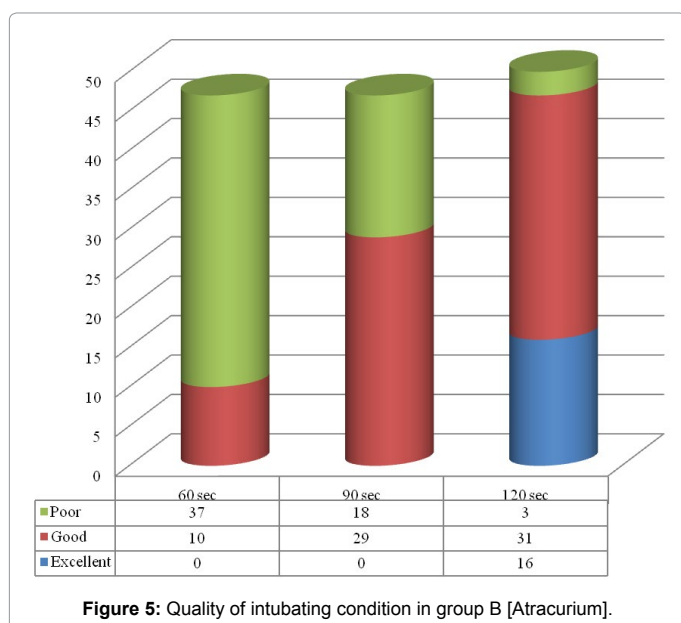


Figure 5: Quality of intubating condition in group B [Atracurium].

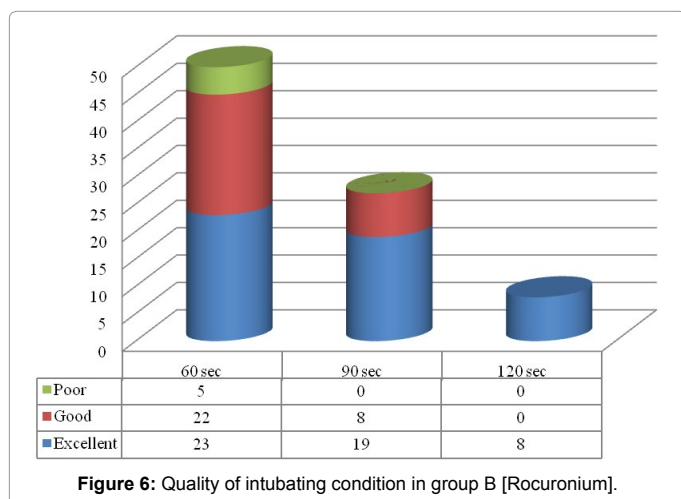


Figure 6: Quality of intubating condition in group B [Rocuronium].

Complete relaxation of the jaw, laryngeal and pharyngeal muscles, and diaphragm are needed for excellent intubating conditions and to reduce the risk of trauma. The response to intubation is a function of both muscular block and the level of anaesthesia. It is possible to intubate a patient with less-than-complete paralysis if a sufficient depth of anaesthesia is present [18]. The authors used same dose of other anesthetics to avoid this confounding. All inhalational anaesthetics have some amount of neuromuscular blocker property [19]. No inhalational anaesthetics and intravenous hypnotic or opioid drugs were used after administration of the neuromuscular blocker. Therefore, it may be supposed that the improvement of intubating conditions results from the increasing neuromuscular block only, with no confounding effects of inhalation agents, opioids or hypnotics. In group C [Rocuronium group] 23 patients out of 50 achieved excellent intubating condition at the end of 60 s, whereas of the 100 patients in the Vecuronium and Atracurium groups, only 4 could have their tracheas intubated 60 s after injection of the neuromuscular blocker, which signifies the faster onset of action with rocuronium.

The onset of neuromuscular block would be faster in centrally located muscles such as the diaphragm, facial, laryngeal, and jaw muscles than peripheral muscles such as the adductor pollicis. The diaphragm, eye muscles, and most laryngeal muscles are more resistant to non-depolarizing relaxants than are peripheral muscles [6]. The diaphragm is resistant to succinylcholine, though the laryngeal muscles are sensitive to it. The masseter muscle is relatively sensitive to both non-depolarizing and depolarizing relaxants. Furthermore, peripheral neuromuscular block was not complete at the time of successful intubation in most patients. In adults, a faster onset at the laryngeal muscle compared to the peripheral muscles was reported with Rocuronium [34], Vecuronium [35] and Atracurium [36]. Therefore, it can be accepted that, when conducting studies of intubating conditions, only frequent-interval intubation attempts, begun sufficiently early can reveal development of optimum laryngeal conditions. This is particularly true for fast-acting neuromuscular blockers, such as Rocuronium, where the peripherally assessed onset of neuromuscular block can give no exact indication of the moment when optimum laryngeal relaxation has first been achieved.

There were few studies where the onset of action of Atracurium was found to be earlier than Vecuronium as reported by [24]. But here in this study, the mean duration of successful intubation after Atracurium (195.43 s ± 1.98 s) is longer than that of Vecuronium (165.46 s ± 1.98 s). These discrepancies might be due to the different techniques of monitoring the neuromuscular blockade used (forced transducer, EMG, etc.) as well as due to the background anaesthetic used.

In most studies, evaluating intubating conditions after Atracurium or Vecuronium, potent inhaled anaesthetics were used during induction, and endotracheal intubation was not attempted until complete neuromuscular block was attained. The results of these studies compares well with the results of the present study. The quality of intubating conditions at the point of successful intubation was also rated better after Rocuronium than with Vecuronium and Atracurium, which matched with the results demonstrated in previous investigations in adults [37]. Vecuronium tended to be superior also to Atracurium, but this difference was not considered statistically significant. In adults, the onset of neuromuscular blockade at the adductor pollicis muscle after Rocuronium is more rapid compared to Vecuronium and Atracurium [25,26] as described. These results match well with the results derived in the present study.

Bartkowski et al. [24] compared the onset, maximal neuromuscular



block, and duration of rocuronium to atracurium and vecuronium during enflurane anesthesia and found significantly faster onset time with Rocuronium. They also found using equipotent doses, atracurium also had a shorter time to develop neuromuscular block than vecuronium. The authors found similar results.

In the atracurium group only 16 patients achieved excellent intubating condition at the end of 120 s and three patients did not reach adequate relaxation even after 240 s. This indicates slower onset and poor quality of relaxation with atracurium than other two drugs. The author thus advocates against use of atracurium where rapid endotracheal intubation are intended such as in critical care settings.

The main limitation of the aforementioned study was the stress response after endotracheal intubation was not adequately addressed. Endotracheal intubation is considered as one of the most stressful procedures and multiple drugs are used to combat the stress related to this procedure of which muscle relaxants assume a crucial part. To assess the stress response, the clinician must address the hemodynamic and clinical parameters (Pulse, blood pressure, electrocardiographic abnormality, papillary changes, etc.) as well as the stress markers (including blood glucose, cortisol and other biomarkers). Another drawback of this study was, the drugs were tested in ideal condition in selected patients posted for elective surgery. For critically ill patients in intensive care units the organ functions (e.g., liver disease, renal failure, etc.) and blood biochemistry (e.g., acid base disturbances, dyselectrolytemias, etc.) are deranged and there is a possibility of altered pharmacokinetics and pharmacodynamics of these drugs. Reversibility of the neuromuscular blockade and duration of action were not addressed in this study. Further studies may be undertaken to consider these possibilities and address the situations [38,39].

## Conclusion

In conclusion, in the aforementioned study, after administration of equipotent doses of vecuronium, atracurium or rocuronium in patients, the speeds with which good intubating conditions were produced were quite different depending on the neuromuscular blocker used. There was more rapid development of clinically acceptable and of better quality intubating conditions after Rocuronium compared to both Vecuronium and Atracurium. So, Rocuronium may be a better choice than Atracurium and Vecuronium for intubation in perioperative as well as critical care settings.

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