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Original Research Article

# Comparative Study on Effect of Rocuronium and Atraconium Induced Rapid Precurarization on Succinylcholine Induced Fasciculations, Post-Operative Myalgias and Intubating Conditions

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**Abstract**

**Background:** Succinylcholine gained widespread use rapidly because of its onset is very fast and duration is ultra-short. However, its utility is compromised due to its adverse effects. succinylcholine-induced muscle fasciculations, myalgia is attenuated and prevented by use of multiple drugs.

**Aims and objectives:** To evaluate the rapid precurarization technique using rocuronium and atracurium induced rapid precurarization on succinylcholine induced rapid fasciculations, post-operative myalgias and intubating conditions.

**Materials and Methods:** A comparative observational study comprising of 60 patients was conducted where selected patients either received ROC 0.1 mg/kg or ATR 0.1 mg/kg, and 10 sec later propofol 2 mg / kg IV was given. A balanced anaesthetic technique was used for all patients. Assessment of fasciculations, myalgia and intubating conditions was done using a 4-point rating scale. All patients were evaluated up to the third postoperative day for the presence of POM.

**Results:** The severity and incidence of post-succinylcholine fasciculations decreased in the ROC group as well as in ATR group. However, significant decrease was observed in ROC group. Similarly, a decrease in the severity and incidence of post-succinylcholine myalgia was observed in both the groups, where ROC group showed significant decrease as compared to ATR group. No significant change in the intubating conditions was observed between both the groups.

**Conclusion:** Severity and incidence of post operative myalgia and fasciculation were significantly decreased by pre-treatment with rocuronium in contrast to atraconium. Hence, ROC is a better option than ATR to combat succinylcholine-related complications like fasciculation and myalgia.

**Keywords:** Myalgia, Fasciculations, Intubation, Succinylcholine, Atraconium, Rocuronium, Non-Depolarizing Muscle Relaxants.

## Introduction

Succinylcholine was discovered by Thesleff, Foldes and associates in 1952" [1]. Succinylcholine plays a vital role in the administration of general anaesthesia during fast sequence intubation because it generates severe and rapid depolarizing neuromuscular block within 30 to 60 seconds, lasting three to five minutes" [2]. Because of its short half-life, it is very important drug during difficult or failed intubation settings.

"However, its usefulness is frequently accompanied by persistent postoperative myalgia (POM)" [3], in addition to a slew of "other side effects such as muscle fasciculations, postoperative myalgia, raised intraocular pressure, intracranial pressure and others limit succinylcholine's utility" [4].

"The prevalence of myalgia induced by succinylcholine ranges between 20% and 80% and often lasts two to three days but can last up to a week" [5]. Several therapeutic measures used for myalgia induced by use of succinylcholine have been recommended, including lignocaine, diazepam, ketorolac, diclofenac, gabapentin, remifentanil, cisatracurium, d-tubocurarine, pancuronium, vecuronium (VEC), rocuronium (ROC), and atracurium. "Pretreatment with a tiny dosage of the non-depolarizing neuromuscular medication prior to succinylcholine administration is the most successful method" [5].

"ROC, unlike all other regularly used non-depolarizing agents, has a very rapid beginning of action and can produce ideal intubating conditions in 60 seconds" [6]. "Pre-treatment with ROC 90 seconds before succinylcholine injection significantly reduces the frequency and intensity of fasciculations" [7]. Based on a randomised trials, meta-analysis, Schreiber *et al* [8] "determined that ROC is NSAIDs drugs are the primary medicines to prevent fasciculation and myalgia caused by succinylcholine."

Till date, there have been very few studies are there for the occurrence and severity of myalgia, fasciculation and intubating conditions post-surgery following succinylcholine administration. Hence, the present research was undertaken to compare the effect of rocuronium and atracurium-induced rapid precurarisation on succinylcholine-induced fasciculations, post-operative myalgias, and intubating conditions.

## Materials and Methods

A comparative observational study was performed at the Department of Anaesthesiology, Index Medical college Hospital and Research Centre, Indore, from January 2020-July 2021 on 60 patients.

Patients of age group 18-55 years, either sex, patients admitted for elective surgeries requiring GA, having ASA score I/II, Mallampati 1 and 2 and without any comorbidity were included in the study. However, patients of age group less than 18 or more than 55, patients having ASA 3 & above, comorbid conditions like: Diabetes mellitus, hypertension, coronary artery disease, Asthma, COPD, renal disease, hepatic disease etc., Suspected difficult intubation, pregnancy, Allergies to drug used, morbidly obese patient, Patient refusal, Emergency surgery were excluded in the study.

Randomization was done by a computer-generated randomization list and allocation was done by sequentially numbered opaque envelopes to one of the two groups. The patients were divided in groups named group A and group B, where each group comprised of 30 patients. Group A patients were administered 0.1mg/kg rocuronium, while group B patients were administered 0.1mg/kg atracurium.

## Anaesthetic technique

**Pre-Anaesthetic evaluation:** Pre-anaesthetic evaluation was done, recording a detailed history, and performing a complete physical examination. Complete blood count, renal function test, blood grouping, random blood sugar, HBsAg, HIV screening test was done. 60 patients within the age of 18 – 55 years undergoing elective surgeries under endotracheal general anaesthesia were randomized into two groups of 30 each. All patients were fasted for 8 hours before the planned surgical procedure. Tab. Diazepam 5mg were given orally on the night before surgery. On the day of surgery two large bore IV cannula were secured and the patients were shifted to the operative room. After obtaining the informed written consent and confirming nil by mouth status patients were received at the operation theatre.

**Premedication:** premedication was done with Inj. Glycopyrrolate 0.004mg/kg Iv,midazolam 0.03mg/kg , ondensetron 0.1mg/kg , fentanyl 2mcg /kg (weight adjusted dose) . Patients SpO2, NIBP, ECG, ETCO2 and heart rate were monitored.

**Preoxygenation:** done with 100% oxygen for 3min via facemask.

**Induction:** Patient is precurarized with 0.1mg/kg Atracurium (group A) or 0.1mg/kg Rocuronium (group B), 10 sec later propofol 2 mg / kg IV was given. At 90 sec succinylcholine at dose of 1.5 mg/kg was injected. Patient intubated at 120 seconds. Laryngoscopy and intubation will be performed using appropriately sized Macintosh blade and after confirmation of bilateral equal air entry, endotracheal tube will be fixed. The patient will be observed for 2 minutes following succinylcholine administration for the presence and severity of fasciculations graded and intubation conditions assessed and graded.

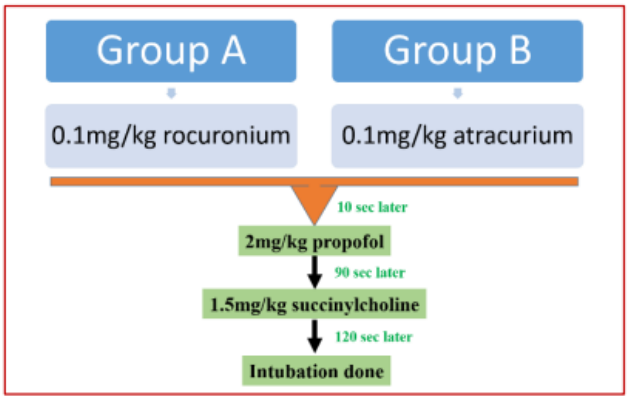


**Figure 1: Anaesthetic technique used in the study.**

Maintenance Anaesthesia will be maintaining with use of 50% nitrous oxide and 50% of oxygen with isoflurane/ desflurane/ sevoflurane. Muscle relaxation was achieved by 0.1mg/kg atracurium iv every 20 min. Not any type of surgical or any other stimulus will be applied during first 10 minutes of study period. Intra operative monitoring of Heart rate, SBP, DBP, MAP, oxygen saturation and EtCO2 recorded every 10 min till discontinuation of drug.

Haemodynamic variables also recorded at specific end point which are baseline, pre-induction, post-induction at 3 min, 5min, 10min, 20min, 30min, 45min, 60min and 120min.

Reversal after surgery completed patients will be reversed with neostigmine 0.05 mg/ kg

body weight and glycopyrrolate 0.008mg/kg. All patients after extubating were shifted to the post anaesthesia care unit at the end of the surgery and were observed. Hemodynamic variables such as heart rate, SBP, DBP, MAP and SpO2 were monitored. All patients evaluated on 6,12,24,48,72 hour for myalgias. Patients evaluated at 2min after succinylcholine for fasciculations.

**Assessment of fasciculations, myalgia and intubating conditions**

The severity of fasciculation was assessed by 4-point scale (Foster, 1960), by an anesthesiologist blinded to the patient's group assignment, where, 0=nil fasciculations; 1=mild, fine fasciculations of the eyes, neck, face, or fingers without limb movement; 2=moderate fasciculations occurring at more than two sites or obvious limb movement; and 3=vigorous or severe, sustained, and widespread fasciculations in the trunk and limbs.

Assessment of intubating conditions: 1) Good –Jaw relaxed, vocal cords wide apart and immobile, no diaphragmatic movement; 2) Adequate – Jaw relaxed, vocal cord apart and immobile, some diaphragmatic movement; 3) Poor-Jaw relaxed, vocal cord moving, marked bucking and coughing.

Myalgia was also graded on a 4-point scale (White, 1962) on day one, day two, and day three postoperatively and was assessed by another investigator who was unaware of the group details, where nil=no muscle pain; mild=muscle stiffness or pain, when specifically enquired in the nape of the neck, or the shoulders and lower chest on deep breathing; moderate=muscle stiffness and pain spontaneously complained of by the patient that needs analgesics; and severe=incapacitating generalized muscle stiffness or pain.

**Statistical Analysis**

IBM SPSS Statistics software version 25.0 (IBM, Armonk, NY) was used for all analyses. All categorical variables were expressed as frequency and percentages. The continuous variables of the data were presented as mean ±standard deviation. The Fisher's exact/chi square test was applied to compare and assess the significance of the difference in the mean values of variables between the two groups. Independent sample t test/ANOVA was used to compare means and standard deviation. A p-value of <0.05 was considered statistically significant.

**Results**

There is No significant differences in terms of age, weight, heart rate, systolic blood pressure, diastolic blood pressure and SPO2 were observed between the two groups as shown in **Table 1.**

**Table1: Baseline characteristics of the study population**

| | Group | | P value |
|---|---|---|---|
| | A | B | |
| Age (year) | 33.63±6.672 | 35.10±7.954 | 0.442 |
| Weight (g) | 51.80±8.160 | 54.50±8.858 | 0.224 |
| HR (b/min) | 75.50±10.153 | 75.23±8.253 | 0.912 |
| SBP (mmHg) | 123.40±8.912 | 123.07±7.534 | 0.876 |
| DBP (mmHg) | 71.27±6.757 | 72.47±7.366 | 0.513 |
| SPO2 (%) | 99.80±.551 | 100.00±.000 | 0.051 |

Data is expressed as **Mean±SD**

In present study, mean duration of action in group A was 55.17±15.114 whereas mean duration in Group B was 56.83±13.293, however no significant In present study, mean duration of action in group A was 55.17±15.114 whereas mean duration in Group B was 56.83±13.293, however no

significant was observed in terms of duration of action between both the groups as revealed by the insignificant p value of 0.652 as shown in Table2.

**Table2: Comparing duration of both the groups.**

| | Group | | P value |
|---|---|---|---|
| | A | B | 0.652 |
| No. of Patients | 30 | 30 | |
| Mean±SD | 55.17±15.114 | 56.83±13.293 | |

In Group A, 40% of the patients had mild fasciculations and 1 (3.3%) had moderate fasciculations whereas in Group B 56.7% had mild fasciculations and 26.7% had moderate fasciculations. There was a significant difference in terms of severity of fasciculations between both the groups as revealed by the significant p value of 0.021. In addition to these findings, there were 17 (56.7%) and 5 (16.7%) patients in Group A and Group B respectively who did not have fasciculations. None of the patients in any group had severe fasciculations as shown in Table3.

**Table 3: Comparing severity of fasciculation.**

| | | Group | | Total | P value |
|---|---|---|---|---|---|
| | | A | B | | |
| Severity of fasciculation | Nil | 16(53.3) | 6(20.0) | 22 (36.7) | 0.021 |
| | Mild | 13 (43.3) | 16 (53.3) | 29 (48.3) | |
| | Moderate | 1 (3.3) | 8 (26.7) | 9 (15.0) | |
| | Severe | 0 (0.0) | 0 (0.0) | 0 (0.0) | |

Data is expressed as percentage (%)

In Group A, majority had good (56.7%) Intubating conditions, 43.3% had adequate intubating conditions, whereas none of the patients had poor intubating conditions. Whereas in Group B, majority had adequate (53.3%) intubating conditions and 46.7% had good intubating conditions. Similar to Group A, no patients had poor Intubating conditions in Group B. It was observed that there was no significant difference observed in terms of intubating conditions between both the groups as revealed by the insignificant p value of 0.438 as shown in Table4.

**Table 4: Comparing intubating conditions.**

| | | Group | | P value |
|---|---|---|---|---|
| | | A | B | |
| Intubating conditions | Good | 17(56.7) | 14(46.7) | 0.438 |
| | Adequate | 13(43.3) | 16(53.3) | |
| | Poor | 0(0.0) | 0(0.0) | |

Data is expressed as percentage (%)

On analyzing post-operative myalgia, at 6 hours mild myalgia was more common in group A (n=16) compared to group B (n=13), p <0.001, whereas moderate myalgia was more common in Group B (half of the patients) compared to group A (n=2). There were significantly more patients who did not have myalgia in group A (n=12) compared to group B (n=2) at 6 hours.

At 12 hours, Mild and moderate both myalgia was more common in group B compared to groups A with p value of 0.011. There were significantly more patients who did not have myalgia in group A (n=16) compared to group B (n=7) at 12 hours.

Similarly at 24 hours, mild myalgia was more common in group B compared to group A (p=0.001). There were significantly more patients who did not have myalgia in group A (n=23) compared to

group B (n=10) at 24 hours. No significant difference was observed in terms of severity of myalgia at 48 and 72 hours between the groups as shown in Table5.

**Table 5: Comparing post-operative myalgia.**

| Time points | Severity | Group A | | Group B | | P value |
|---|---|---|---|---|---|---|
| | | Frequency | Percentage | Frequency | Percentage | |
| 6 | Nil | 12 | 40 | 2 | 6.7 | <0.001 |
| | Mild | 16 | 53.3 | 13 | 43.3 | |
| | Moderate | 2 | 6.7 | 15 | 50 | |
| 12 | Nil | 16 | 53.3 | 7 | 23.3 | 0.011 |
| | Mild | 14 | 46.7 | 18 | 60 | |
| | Moderate | 0 | 0 | 5 | 16.7 | |
| 24 | Nil | 23 | 76.7 | 10 | 33.3 | 0.001 |
| | Mild | 7 | 23.3 | 20 | 66.7 | |
| | Moderate | 0 | 0 | 0 | 0 | |
| 48 | Nil | 25 | 83.3 | 20 | 66.7 | 0.136 |
| | Mild | 5 | 16.7 | 10 | 33.3 | |
| | Moderate | 0 | 0 | 0 | 0 | |
| 72 | Nil | 29 | 96.7 | 26 | 86.7 | 0.161 |
| | Mild | 1 | 3.3 | 4 | 13.3 | |
| | Moderate | 0 | 0 | 0 | 0 | |

## Discussion

"The efficacy of the pre-treatment is determined by the choice of the non-depolarizing agent" [9], the extent of prejunctional receptor block, the time gap between the administration of the pre-treatment agent and succinylcholine, and the speed of onset of the non-depolarising drug. "Rocuronium and atracurium were described as the primary pre-treatment agent in preventing succinylcholine-induced fasciculations and post-operative myalgia" [10]. In view of this, we did a study to compare rocuronium with atracurium.

In a study conducted by Senapati *et al*. [5] "mean age observed was 39.45 ± 11.85 which was comparable to our study results of 33.63±6.6 mean age". Amin *et al*. 2009 found that "hemodynamically, rocuronium did not exert significant changes, but the interaction of the relaxants and the anaesthetic agents resulted in statistically significant decline in some hemodynamic parameters at certain periods which are not clinically significant and required no medications" [11]. Módolo *et al*. showed that "rocuronium and atracurium had also not determined significant hemodynamic changes" [12].

Patel *et al*. observed good hemodynamic stability with no statistically significant increase in pulse rate, systolic and diastolic arterial blood pressure following intravenous rocuronium bromide administration. "Rocuronium bromide can therefore be advocated as the drug of choice in elective as well as in emergency surgery where rapid intubation will be beneficial without compromise of hemodynamic stability" [13].

Mild and moderate fasciculations were more in atracurium group B as compared to rocuronium group A. In the group A, incidence of mild fasciculation was 40.0% (n=12) and that of moderate was 3.3% (n=1), while in group B, it was 56.7% (n=17) and 26.7% (n=8) respectively. In addition to these findings, there were 17 (56.7%) and 5 (16.7%) patients in Group A and Group B respectively who did not have fasciculations.

None of the patients in any group had severe fasciculations.

Farhat *et al* found that the "frequency of fasciculations with rocuronium pre-treatment group (23.2%) to be significantly less than with no pre-treatment group (100%, p< 0.001)" [14]. Similarly, Ban C.H. Tsui found the "incidence of fasciculations in the rocuronium group (21.4%) was lower (P < 0.001) than in the atracurium (78.5%) or placebo (92.8%) groups" [15]. Abbas *et al* also reported that "fasciculations were noticed in group A placebo as 100% (mild to severe) and in group B rocuronium 0.1mg/kg pre-treatment group 13.3% (mild)" [10].

It was observed that the efficacy of preventing succinylcholine-induced fasciculation's relies upon the level of affinity of non-depolarizing muscle relaxants for prejunctional choline receptors. Higher affinity was found with rocuronium, which explains its better effectiveness.

In a study conducted by Joshi *et al*. "the incidence of fasciculations was 24% with rocuronium, with a 100% incidence rate in the control group (normal saline)" [13].

Schreiber *et al*. reported "postoperative myalgia and fasciculation after use of succinylcholine are a well-recognized side effect with the reported incidence of 50% and 95%, respectively" [8]. Kim *et al* reported the "incidence and severity of visible muscle fasciculation was significantly less with increasing the amount of precurarizing dose of rocuronium (P < 0.001)". Those of myalgia tend to decrease according to increasing the amount of precurarizing dose of rocuronium, but there was no significance (P = 0.072). "The onset time of succinylcholine was significantly longer with increasing the amount of precurarizing dose of rocuronium (P < 0.001)" [16]. Our findings are in line with all the above studies.

In our study, it was observed that pre-treatment with either rocuronium or atracurium provided good intubating conditions without any statistically significant difference, with an overall intubation condition good to adequate in every patient of both groups.

Tsui *et al*. [15], O'Sullivan *et al*. [17], Pendeville *et al*. [18], Venkateswaran *et al*. [19] and Eikermann *et al*. [20] utilized comparison of rocuronium with atracurium, mivacurium, vecuronium or placebo pre-treatment before the administration of succinylcholine for endotracheal intubation. They could not find any dissimilarity in intubation conditions in their patients, which endorse the findings of our study.

On analyzing post-operative myalgia, at 6 hours mild myalgia was more common in group A (n=16) compared to group B (n=13), p<0.001, whereas moderate myalgia was more common in Group B (n=15) compared to group A (n=2). At 12 hours, mild and moderate each myalgia was more common in group B compared to groups A with p value of 0.011. Similarly at 24 hours, mild myalgia was more common in group B compared to group A (p=0.001). However, there were no significant difference observed in terms of severity of myalgia at 48 and 72 hours between the groups.

In a study by Senapati *et al*, it was reported that POM decreased significantly in the ROC group than in the VEC group. The incidence of POM on day two was significantly less in both groups. There was no statistically significant difference between the two groups based on Fischer's exact test (p=1.000). "The myalgia on postoperative day two and day three did not show any statistical significance between the two groups" [5].

Our results are consistent with those of O'Sullivan *et al*. [17] and Erkola [21]. Findlay and Spittal [22] found "no statistically significant difference in the occurrence of

myalgia on the third postoperative day between the ROC and VEC groups, which is consistent with our findings.

Waters and Mapleson [23] propose that "myalgia is caused by muscle injury caused by unsynchronized contraction of nearby muscle fibres right before paralysis, resulting in shearing of connective tissues, as well as the release of prostaglandins and electrolyte imbalance". Yet, numerous researchers have failed to explain the link between fasciculations and myalgia. As a result, pre-treatment with non-depolarizing drugs reduces the negative effect of succinylcholine at the neuromuscular junction.

## Conclusion

The severity and occurrence of mild to moderate fasciculations were less in the rocuronium group in contrast with the atracurium group. Both drugs rocuronium and atracurium produced excellent intubating conditions.

Similarly, the incidence and seriousness of mild to moderate post-operative myalgia were significant on second postoperative day, being more common in atracurium group compared to rocuronium group. However, no patients complained of myalgia on the third postoperative day.

Our observation is that rocuronium is cost-effective due to reduced postoperative analgesic requirements. Even though it is not standard practice, the use of rocuronium is advocated before succinylcholine to negate the side effects while taking advantage of its plethora of benefits in various elective surgeries.

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