ORIGINAL ARTICLE

Rapid sequence induction and intubation with succinylcholine and rocuronium with priming - A comparative study

Sheikh Faraz Jelani, Neeharika Arora, Pallavi Ahluwalia, Ankur Garg, Mohd Khalik, Ishan Verma

Department of Anesthesia, Rohilkhand Medical College, Bareilly, Uttar Pradesh, India

Corresponding Author:
Dr. Ankur Garg, Department of Anesthesia, Rohilkhand Medical College, Bareilly, Uttar Pradesh, India.
E-mail: farazleo555@gmail.com

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Background: The administration of skeletal muscle relaxants in general anesthesia produces muscular relaxation and attenuation of protective airway reflexes, leaving the airway exposed from induction till effective intubation. **Materials and Methods:** This randomized prospective comparative blinded clinical study was carried out after approval from Institutional Ethical Committee and informed consent. Adult patients American Society of Anesthesiologists I and II, posted for elective surgery under General Anaesthesia were included. Patients were randomly divided and recruited into two groups. Group A: Patients received 1ml normal saline followed 1.5 mg/kg of succinylcholine diluted in 5 ml after 2.5 min. Group B: Patients received 0.06 mg/kg rocuronium diluted in 1 ml and followed by 0.54 mg/kg of rocuronium diluted in 5 ml after 2.5 min. Onset time of neuromuscular blockade was noted. The trachea was intubated by appropriately sized PVC cuffed endotracheal tube after direct laryngoscopy, quality of intubating condition was assessed by Cooper *et al*. scoring system. Intraoperatively multipara monitoring was done. Side effects, if any were noted. **Results:** Both the groups were comparable in terms of demograhic profile. There was no significant difference in the Intubating condition in both the groups. Mean Onset of neuromuscular blockade (seconds) of the patients in the group A was less as compared to Group B but it was not statistically significant. Mean duration of action of loading dose (min) of patients in Group A was less as compared to Group B and was statistically significant ($P < 0.001$). There was no significant difference in mean intubating score. There was a significant difference in mean heart rate of patients at induction, at intubation and at 5 min in both the groups. **Conclusion:** The study, therefore, confirms that in a variety of conditions where succinylcholine is contraindicated, rocuronium with priming can act as a fine alternative.

KEY WORDS: General anesthesia, N-methyl-D-aspartate, Rapid sequence intubation, Rocuronium, Succinylcholine

INTRODUCTION

The administration of skeletal muscle relaxants in general anesthesia produces muscular relaxation and attenuation of protective airway reflexes in order to facilitate endotracheal intubation. Rapid-sequence intubation (RSI) is a technique for swiftly securing an airway in patients who are at risk of aspiration, have an impending airway loss in situations like acute burns or trauma, or who require mechanical ventilation due to significantly compromised gas exchange.[1] Rapid onset of action, short duration of action, minor hemodynamic effects, minimal side effect profile, and swiftly reversible are all desirable pharmacokinetic qualities for all RSI medicines.[2]

Succinylcholine, a depolarising muscle relaxant is the drug of the choice for RSI in a dose of 1–2 mg/kg as it provides muscle

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relaxation in 60–90 s. Rocuronium has been shown in several clinical investigations to have no cardiovascular side effects and to have no histamine-releasing capability minor vagolytic effects. Due to its faster distribution to the action site in the laryngeal muscles as compared to vecuronium. Rocuronium has a rapid onset time, which allows for tracheal intubation within 60 s of administration.[3]

From previous studies, it is also observed that rocuronium of 0.6 mg/kg dose provides good intubating conditions in 90 s whereas succinylcholine 1.5 mg/kg provides good intubating conditions in 60 s.[4] The priming principle refers to the administration of a doses (10% of the intubating doses) of a nondepolarising relaxant, which when followed by the remaining intubating dose after 2.5 min produces relatively rapid and profound blockade to ensure suitable condition for endotracheal intubation.[5] Priming improves the time of onset and intubating conditions when rocuronium is administered in dose of 0.6 mg/kg.[5]

Here, in our study, we had compared the onset time and intubating condition in two muscle relaxant drugs namely succinylcholine and rocuronium with priming.

MATERIALS AND METHODS

Randomized prospective comparative blinded clinical study carried out after approval from Institutional Ethical Committee (IEC/59/2019/SEPT), CTRI registration (CTRI/2020/03/023864) and consent from study participants. Adult patients posted for surgery under general anesthesia were included in the study. Patients with an anticipated difficult airway, eye surgery, hyperkalemia, duchene muscular dystrophy, close angle glaucoma, severe liver diseases, bradycardia, rhabdomyolysis, and with history of malignant hyperthermia were excluded from the study.

Patients were randomly divided and recruited into two groups in equal numbers, i.e., Group A and Group B, according to a computer-generated randomized chart [Figure 1]. Group A: Patients received 1 ml normal saline followed 1.5 mg/kg of succinylcholine diluted in 5 ml after 2.5 min. Group B: Patients received 0.06 mg/kg rocuronium diluted in 1 ml and followed by 0.54 mg/kg of rocuronium diluted in 5 ml after 2.5 min. After the patient was received into operation rooms, multiparameter (space lab medicals, Redmund, USA) was attached. 18G intravenous (IV) cannula was inserted in non-dominant hand. IV fluid (Ringer lactate) was started and after recording baseline vital parameters, two electrodes were attached on the ulnar surface of the forearm 2 cm above the palmar crease for attaching neuromuscular monitor.

Digistim III (neurotechnology I.N.C, Texas, USA) was used to monitor neuromuscular blockade and the ulnar nerve was stimulated to see twitching of muscle adductor pollicis at the thumb. Supramaximal current was determined.

After premedication with injection. Glycopyrrolate 0.2 mg i.v., ondansetron 4 mg i.v., and butorphanol 1 mg i.v., pre-oxygenation for 3 min was done with 100% oxygen. Induction was done with injection. propofol 2.0 mg/kg i.v., and after confirming hypnosis. Group A patients received 1 ml normal saline followed 1.5 mg/kg of succinylcholine diluted in 5 ml after 2.5 min. and Group B patients received 0.06 mg/kg rocuronium diluted in 1 ml and will give 0.54 mg/kg of rocuronium diluted in 5 ml after 2.5 min.

Stimulation by single twitch supramaximal current of 1 Hz frequency was given and loss of response, i.e., thumb twitch to supramaximal current was considered as onset time and laryngoscopy was then performed. The trachea was intubated by proper size PVC cuffed endotracheal tube by direct laryngoscopy, quality of intubating condition was assessed by Cooper *et al*. scoring system[6] [Table 1] and was graded as poor, nominal, moderate, good.

Anesthesia was maintained with a mixture of nitrous oxide, oxygen, isoflurane (0.8–1%), and intermittent positive pressure ventilation. Systolic blood pressure (SBP), diastolic blood pressures (DBPs), mean arterial pressures (MAPs), and the pulse rate, $ETCO_2$ were therefore recorded at the time of the muscle relaxant injection and at 5 min and 10 min after the injection. Duration of loading dose was calculated as time from injection of relaxant until the return of diaphragm movement or appearance of curare cleft in ETCo2 (criticare system ING North Kingston, USA). To maintain neuromuscular blockade vecuronium 0.03 mg/kg was given intermittently throughout the surgery. Reversal was done by neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg) mixture administration. After adequate reversal, the patient was shifted to the room of recovery for post-operative monitoring.

RESULTS

The mean age of Group A patients was 39.57 ± 13.43 years and in Group B was 37.2 ± 11.81 years. There were 16 male and 14 female patients in Group A and 17 male and 13 female patients in Group B [Table 2]. Out of 30 patients in Group A all 30 patients have Excellent (8–9) Intubating condition and in Group B maximum 27 have Excellent (8–9) and 3 have Good (6–7) Intubating condition and difference is not significant in Intubating condition of patients in between Group A and Group B [Figure 2]. Mean onset of neuromuscular blockade (seconds) in Group A patients was 61.47 ± 4.55 s and in Group B was 62.47 ± 3.79 s [Table 3]. Mean Onset of neuromuscular blockade (seconds) of Group A patients was less as compare to Group B and the difference is not significant in mean onset of neuromuscular blockade (seconds) of patients in between Group A and Group B. Mean duration of loading dose (min) of patients in Group A was 7.27 ± 0.74 min and in Group B was 33.43 ± 5.28 min [Figure 3]. Mean duration of loading dose (min) of patients in Group A was less as compared to Group B. There was a significant difference in mean duration of loading dose (min) of patients in between Group A and Group B ($P < 0.001$). Mean intubating score of Group A patients was 8.13 ± 0.35 and in Group B was 8.27 ± 0.64 [Table 4]. No significant difference was found in mean intubating score of patients in between

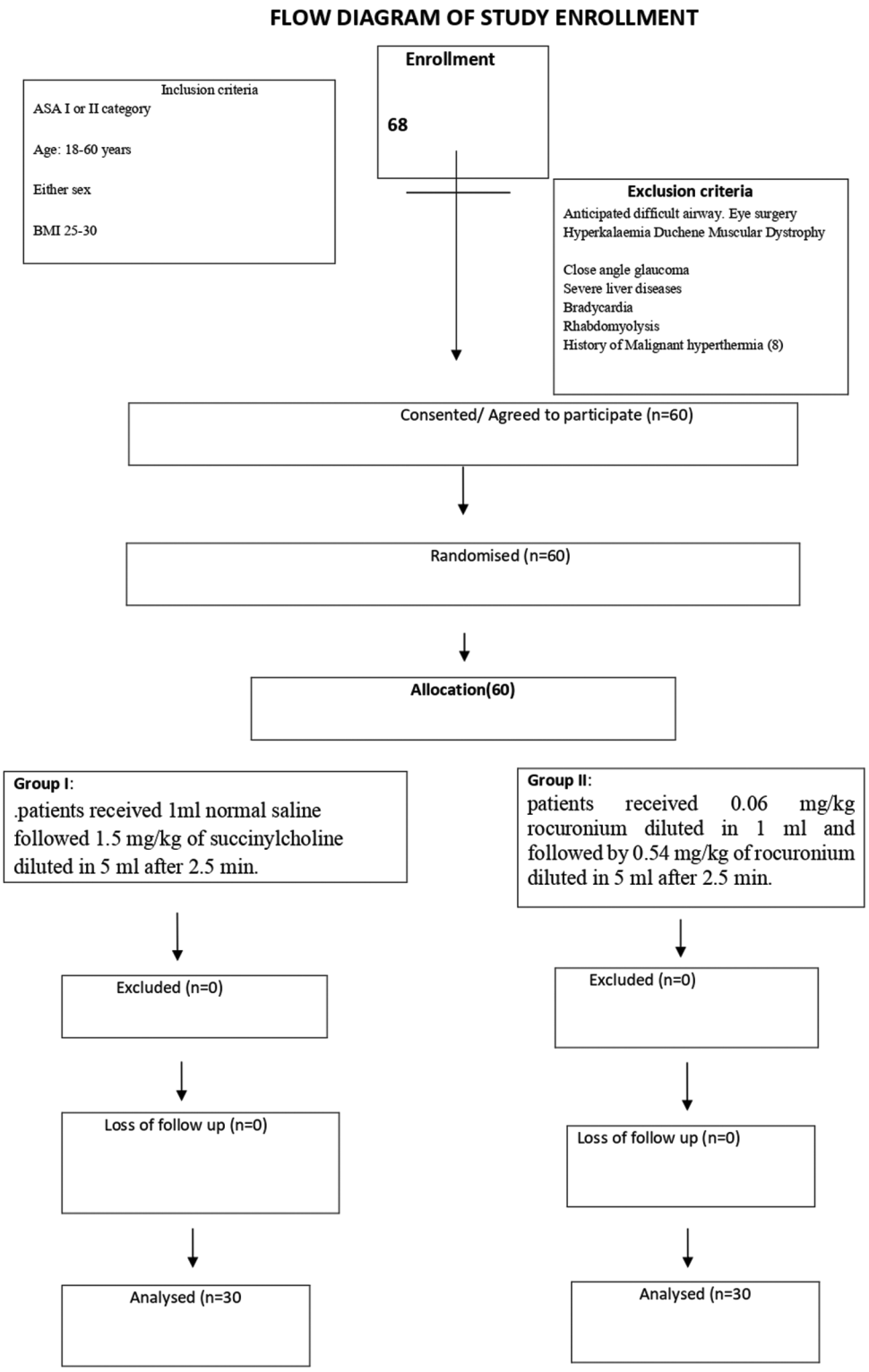

Figure 1: Consort flow diagram for study enrollment

Group A and Group B. Mean heart rate of Group A patients at baseline was 68.23 ± 5.72 and in Group B was 71.9 ± 12.01. Mean heart rate of Group A patients after premedication was 64.13 ± 4.94 and in Group B was 66.43 ± 9.99. Mean heart rate of Group A patients on Induction was 58.87 ± 4.77 in Group B was 64.03 ± 11.07. Mean heart rate of Group A patients on intubation was 74.4 ± 15.14 and in Group B was 66.63 ± 3.76. Mean heart rate of Group A patients at 5 min was 62.93 ± 3.51 and in Group B was 68.0 ± 12.47. Mean heart rate of Group A patients at 10 min was 60.53 ± 3.78 and in Group B was 64.37 ± 10.27. There was no significant difference in mean heart rate of patients at baseline, after premedication and at 10 min in between Group A and Group B. The difference was significant in mean heart rate of patients at induction, at intubation and at 5 min in between Group A and Group B. Mean SBP of Group A patients at baseline was 130.53 ± 2.67 and in

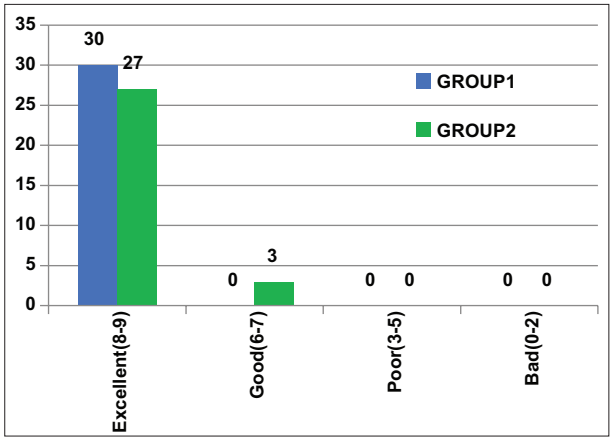

Figure 2: Comparison of intubating condition of patients in both groups

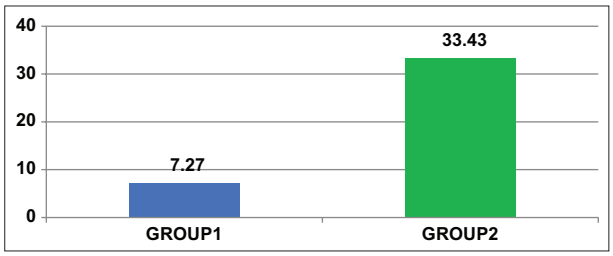

Figure 3: Comparison of mean duration of loading dose (min) in between Group A and Group B

Group B was 129.83 ± 6.61. Mean SBP of Group A patients After premedication was 122.97 ± 4.78 and in Group B was 124.9 ± 4.87. Mean SBP of Group A patients on induction was 122.0 ± 2.46 and in Group B was 122.4 ± 7.18. Mean SBP of Group A patients on intubation was 132.2 ± 1.77 and in Group B was134.4 ± 9.16. Mean SBP of in Group A patients at 5 min was 127.37 ± 1.5 and in Group B was 126.8 ± 8.62. Mean SBP of Group A patients at 10 min was 122.8 ± 5.55 and in Group B was 120.63 ± 6.65. Significant difference was not seen in mean SBP of patients at baseline, After premedication at induction, at intubation, at 5 min and at 10 min in between Group A and Group B. Mean DBP of Group A patients at baseline was 80.07 ± 2.41 and in Group B was 79.57 ± 6.73. Mean DBP of Group A patients After premedication was 76.27 ± 2.69 and in Group B was 75.63 ± 5.96. Mean DBP of Group A patients on Induction was 72.7 ± 1.99 and in Group B was 73.37 ± 7.69. Mean DBP of Group A patients on intubation was 74.8 ± 9.55 and in Group B was 74.8 ± 9.55 76.73 ± 2.43. Mean DBP of Group A patients at 5 min was 74.3 ± 2.77 and in Group B was 71.03 ± 8.06. Mean DBP of Group A patients at 10 min was 72.17 ± 3.79 and in Group B was 70.13 ± 7.31. Significant difference was not found in mean DBP of patients at baseline, After premedication at induction, at intubation, at 5 min and at 10 min in between Group A and Group B. Mean MAP of Group A patients at baseline was 93.89 ± 2.4 and in Group B was 92.32 ± 5.54. Mean MAP of Group A patients after premedication was 88.5 ± 10.77 and in Group B was 88.06 ± 4.49. Mean MAP of Group A patients on Induction was 86.13 ± 1.55 and in Group B was 85.71 ± 6.69. Mean MAP of patients in Group A on intubation was 95.22 ± 2.0 and in Group B was 94.67 ± 8.39.

Table 1: Cooper *et al.* scoring system

Score	Jaw relaxation	Vocal cord	Response to intubation
0	Poor	Closed	Severe coughing/bucking
1	Nominal	Closing	Mild cough
2	Moderate	Moving	Slight diaphragmatic movement
3	Good	Open	None

Table 2: Comparison of two groups

Variable	Group A	Group B	*P*-value
Age in years (Mean±SD)	39.57±13.43	37.2±11.81	0.471#
Sex			
Male	16	17	0.795#
Female	14	13	
ASA Grade			
I *n* (%)	24 (80)	25 (83.3)	0.793#
II *n* (%)	6 (20)	5 (16.7)	

#Statistically not significant, ASA: American Society of Anesthesiologists

Table 3: Comparison of onset of neuromuscular blockade (seconds) in between Group A and Group B

Variable	Group A	Group B	*P*-value
	Mean±SD	Mean±SD	
Onset of neuromuscular Blockade (seconds)	61.47±4.55	62.47±3.79	0.358

#Statistically not significant

Table 4: Comparison of intubating score in between Group A and Group B (Based on Cooper *et al.* scoring)

Variable	Group A	Group B	*P*-value
	Mean±SD	Mean±SD	
intubating score	8.13±0.35	8.27±0.64	0.319#

#Statistically not significant

Mean MAP of Group A patients at 5 min was 91.32 ± 2.22 and in Group B was 90.96 ± 7.29. Mean MAP of Group A patients at 10 min was 89.71 ± 2.94 and in Group B was 88.63 ± 6.38. Significant difference was not found in mean MAP of patients at baseline, After premedication at induction, at intubation, at 5 min and at 10 min in between Group A and Group B.

Individual scores were added to give overall intubation score. An intubation score 8–9 consider as excellent, 6–7 was good, 3–5 was poor and 0–2 was bad. The good to excellent intubation score taken as clinical acceptable.

DISCUSSION

Following ablation of protective airway reflexes with induction of anesthesia, RSI is used to secure a definitive airway in the shortest period of time. Succinylcholine plays a role in RSI, but it has been linked to a number of side effects. The study aims to

evaluate and compare the onset and conditions of intubation in succinylcholine and rocuronium with priming.

The present prospective cross-sectional study included adult patients belonging to the American Society of Anesthesiologists (ASA) I or II category, who had been admitted to the hospital for surgery requiring the general anesthesia and the intubation of the trachea. Any patient belonging to ASA III or beyond was not included so as to avoid incorporation of any bias in the results arising from the physical condition of the patient.

The mean onset of neuromuscular blockade in Group A patients was 61.47 ± 4.55 s and in Group B was 62.47 ± 3.79 s in the study. The mean onset of action in Group A patients was comparable to Group B. The present study has utilized the scoring system for assessing intubating condition by Cooper *et al*. as it is widely accepted amongst scientific researchers.[6]

Out of 30 patients in Group Succinylcholine, it was observed that all 30 patients had Excellent (score ranging between 8 and 9) intubating condition and in Group rocuronium 27 have Excellent (8–9) and 3 have Good (6–7) intubating condition. No statistically significant difference was observed here. Mean intubating score of Group succinylcholine patients was 8.13 ± 0.35 and in Group Rocuronium was 8.27 ± 0.64. No significant difference was found in mean intubating score of patients in between Group succinylcholine and rocuronium with priming.

The result is in accordance with the findings of Cooper *et al*. who reported comparable intubating conditions following administering Org 9426 (rocuronium) 600 mg/kg at 60 or 90 s to groups of 20 patients anesthetized with thiopentone, nitrous oxide in oxygen, and modest doses of fentanyl and thereafter compared the data to those obtained after giving suxamethonium 1 mg/kg to similar groups of patients.[6]

The intubating conditions were excellent in 65% of patients at 60 s and 85% at 90 s with rocuronium while a greater no. of patients had excellent intubating conditions at 60 s with the use of succinylcholine. The onset time of succinylcholine was much faster than rocuronium which explains the difference between incidence of excellent intubating conditions at 60 s and 90 s with the use of rocuronium. In our study, we attempted intubation only at the time of onset which was similar in both groups, and found intubating conditions excellent in 90% of patients.

Sridhar *et al*.[7] evaluated and compared three different dosage techniques including priming dose of 0.06 mg/kg of rocuronium followed by 0.54 mg/kg rocuronium 3 min later, 0.06 mg/kg followed by 0.54 mg/kg rocuronium 2 min later, and saline followed by 0.6 mg/kg rocuronium 3 min later. They described the onset times of intubation as 57.4 ± 16.3 s in patients who received a priming dose of 0.06 mg/kg of rocuronium followed by 0.54 mg/kg rocuronium 3 min later, 104.8 ± 11.5 s in the ones who were administered with 0.06 mg/kg followed by 0.54 mg/kg rocuronium 2 min later, and 123.9 ± 13 s in the control group who were injected with saline followed by 0.6 mg/kg rocuronium 3 min later. Their study concluded that in <60 s, rocuronium's 3-min priming time affords ideal intubating circumstances.[7]

The authors concluded that all the three interventions had comparable intubating conditions that proved to be good for general anesthesia when intubation was attempted after loss of T1 on train-of-four (TOF) monitoring.[7]

Rocuronium priming provides the advantage of earlier onset over rocuronium. They have not compared rocuronium with priming to succinylcholine. In our study, the priming interval was 3 min, and intubation was attempted at loss of single twitch to supramaximal stimulus at adductor pollicis, and we observed that intubating conditions on priming with rocuronium were comparable to succinylcholine, and the time to onset was comparable with succinylcholine. Thus, our results corroborate with the said study.

Singh *et al*.[8] also stated of observing comparable intubating conditions in two different groups of 0.6 mg/kg rocuronium and 1.5 mg/kg suxamethonium when compared in 40 patients (n = 20 for each group) at 60 s found no significant difference in intubating conditions that were clinically acceptable,[9] in spite of rocuronium having a longer time to achieve maximum blockade as noted by time taken to maximum suppression of twitch response to the supramaximal stimulus. A statistically significant difference in the onset of action between succinylcholine and rocuronium was reported and it was mentioned that with 0.6 mg/kg rocuronium and 1.5 mg/kg succinylcholine, the time to achieve maximum blockade was 87.94 s and 65.59 s respectively.[8]

The time of intubation was not same as time of maximum blockade. The intubating conditions 60 s after the injection of relaxant, were found to be comparable. In our study time of maximum blockade was considered as time of onset which was comparable in the two groups and both succinylcholine and rocuronium were equally effective in achieving acceptable intubating conditions.

In a study by Misra *et al*.[9] the authors described that the mean time for the onset of action of succinylcholine (1.5 mg/kg) as 46.69 ± 14.78 s, for rocuronium (0.6 mg/kg) it was 53.67 ± 11.87 s, and for vecuronium (0.1 mg/kg^{-1}) the value was 78.2 ± 14.89 s when evaluated and compared in 90 patients (n = 30) aged between 16 and 60 years.[9]

They found no significant difference between succinylcholine and rocuronium in terms of time of onset based on clinical criteria. Misra *et al*.[9] reported that succinylcholine and rocuronium produced comparable yet superior conditions when compared to vecuronium at 90 s following administration of the respective drugs.

The intubating conditions when compared at 60 s were superior most with the succinylcholine providing excellent conditions in 90% of patients followed by rocuronium which gave excellent intubating conditions in 70% though the intubating conditions

were acceptable in 90% of patients.[9] In our study, the intubating conditions were comparable in both succinylcholine and rocuronium groups as well as the time of onset based on loss of response to the supramaximal stimulus at adductor pollicis.

Another study that determined the benefits of priming effect was the one conducted by Rao *et al*.[5] In one group, the authors employed a 0.06 mg/kg rocuronium priming dosage, followed by 0.54 mg/kg rocuronium 3 min later. The control group got saline followed by 0.6 mg/kg rocuronium. The priming group had a 50.6 ± 7.4 s onset time whereas the control group had a 94.0 ± 11.62 s onset time which was statistically significant.

The intubation score was 8–9 in both the groups signifies excellent grade, when intubation was attempted at loss of T1 on TOF.[5] We observed rocuronium with priming provided intubation score similar to succinylcholine at the time of onset defined by loss of which supramaximal stimulus, though it was achieved by rocuronium with priming group at time comparable to succinylcholine.

In a similar study by Griffith *et al*.[10] reported earlier onset at 34 ± 6 s in the priming group that received rocuronium 0.06 mg/kg 2 min prior to rocuronium 0.54 mg/kg than 59 ± 14 s in the group that received rocuronium 0.6 mg/kg without priming.

The intubating conditions in the two groups were found to be adequate and comparable. The onset of neuromuscular block was accelerated with the use of rocuronium with priming. Previous studies have established that priming with rocuronium provides the advantage of earlier onset over rocuronium 0.6 mg/kg without compromising the intubating conditions. Though this technique has not been compared to succinylcholine. We have found that rocuronium with priming as effective as succinylcholine in terms of both onset and intubating conditions.

The study results demonstrate that the mean duration of loading dose of patients in Group Succinylcholine was 7.27 ± 0.74 min and in Group Rocuronium was 33.43 ± 5.28 min, the difference being statistically significant.

Similar results for rocuronium drug were established in the study by Griffith *et al*.[10] who studied if priming with rocuronium (0.06 mg/kg) followed by intubating dose of 0.54 mg/kg accelerates the neuromuscular blockade onset. The clinical duration of action and the recovery index did not show any statistically significant difference between the two groups with values of 32 ± 17 min and 29 ± 19 min for rocuronium used with and without priming respectively. Hence, the duration of action for rocuronium with priming as observed in the present study is comparable to that of Griffith *et al*.'s observed value.[10]

Ajeet *et al*.[8] compared 0.6 mg/kg rocuronium and 1.5 mg/kg suxamethonium in groups of 20 patients. The observed duration of action of suxamethonium and rocuronium was 318 s and 1705.8 s, respectively.[8] The results for succinylcholine are comparable to that of the present study but that of rocuronium is significantly less than that observed currently.

In the study by Cooper *et al*.[6] wherein the authors compared circumstantial parameters following ORG (rocuronium 0.6 mg/kg) administration in group of 20 patients and the data obtained after suxamethonium (1 mg/kg) administration in similar groups of patients, 90% recovery from suxamethonium block occurred by 13.3 min, whereas clinical relaxation (time to 25% recovery) took 30.5 min with Org 9426.[6] The author reported that as they have not observed a biphasic block and took into consideration only the initial rapid phase, hence their results vary from contemporary studies.[6]

Sridhar *et al*.,[7] Misra *et al*.[9] and Rao *et al*.[5] however did not mention about the duration of action of loading dose in their studies.

The present study has certain strengths and limitations. The small sample size of the present study is a limitation as a larger sample would be ideal for more clarity of the results. Moreover, the study did not bring into consideration the possible outcomes of rocuronium when used without priming. However, even though studies have reported comparison between succinylcholine, rocuronium, and other drugs such as vecuronium and those between plain rocuronium and one with priming, there is no study that has yet recorded the comparison of succinylcholine with rocuronium priming. Hence the unique nature of the study is appreciated.

CONCLUSION

The study, therefore, concludes from its observations that rocuronium is a newer and comparable alternative to succinylcholine and especially effective if administered following the priming principle. The former may very well be used in cases where succinylcholine is contraindicated. It can be a good alternative in entire scenario where succinylcholine is contraindicated.

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