

Comparative study of inj. Rocuronium with priming dose and inj. Rocuronium without priming with respect to onset, time of intubation and intubating conditions in patients undergoing general anaesthesia

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Abstract

Background: Rocuronium is fastest among non-depolarizing muscle relaxants, but still it produces appropriate intubating conditions comparable to succinylcholine, in >90 seconds on administering 2 × ED₉₅ dose as a bolus dose. In present study we compared the effect of inj. Rocuronium with priming dose and inj. Rocuronium without priming on intubating conditions and onset time of intubation with respect to rocuronium as bolus. **Material and Methods:** Present study was single-center, prospective, randomized study, conducted in patients of age groups from 18-60 years of either sex, 40-60 kgs weight, ASA grades I and II, undergoing surgeries under general anaesthesia and given valid written consent for participation. The patients were randomly allocated into 2 groups of 30 patients each as Group C (control group) and Group P (priming group). **Results:** Overall, 60 patients were studied in age group of 18 to 60 years, 30 patients in each group C and group P. we compared mean age, weight, gender and ASA grade between group C and group P and difference was statistically not significant (p value >0.05). We compared mean HR, mean MAP and mean SPO₂ preoperatively baseline, at induction, at intubation, mean HR at 1 minute after intubation and mean HR at 5 minute after intubation between group C and group P, the difference between two groups was statistically insignificant. (P value >.05) In group C, out of 30 patients, 17 patients were having score 9 while 12 patients were having score 8, while 1 patient had score 7 which was comparable with the group P in which out of 30 patients, 18 were having score 9, while 11 patients were having score 8 and 1 patient was of score 7, so in both groups most of the patients (96.67% in each group) had excellent intubating condition, and the groups were comparable as statistically no significant difference was noted. In group C mean Onset Time of Intubation was 92.33 ± 6.26 seconds, while in group P it was 56 ± 6.75 seconds, so the difference between the groups on the basis of OTI was statistically highly significant. (P value 0.0001) **Conclusion:** Rocuronium with priming would be an excellent alternative to succinylcholine, whenever fast induction will be needed. Intubating conditions were good to excellent and comparable in both rocuronium with priming and without priming. NMT monitoring is a useful tool for indicating the clinically acceptable paralysis.

Keywords: Rocuronium, priming dose, Intubating conditions, general anaesthesia

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INTRODUCTION

General anaesthesia is a practice known since long time to anaesthetise the patient for surgeries. In routine it involves induction and intubation which mostly involves non-depolarizing agent as a muscle relaxant which takes 3-4 minutes to provide appropriate intubating conditions depending on the agent. But at times faster induction and intubation is needed, like in emergency conditions or when patient is full of gastric contents for which we have to use

some agent which provide such conditions relatively faster. Since long time Succinylcholine is best known and used for faster induction in anaesthesia including rapid sequence intubation. It is a depolarizing type of muscle relaxant. It is known for producing good to excellent intubating conditions, in very less time (onset time of intubation 30- 60 seconds).¹ But it is found to be associated with certain side effects like muscle fasciculations, myalgia, hyperkalemia², bradyarrhythmias³, increased intracranial tension⁴, increased intra ocular tension, malignant hyperthermia, increased intragastric pressure and sustained muscle spasm. Rocuronium is fastest among non-depolarizing muscle relaxants, but still it produces appropriate intubating conditions comparable to succinylcholine, in >90 seconds on administering 2 × ED95 dose as a bolus dose.^{5,6} So there is a need for reducing the onset time of intubation further which should be better or at least comparable to succinylcholine, aiming this goal we have used the priming principle with the rocuronium and compared the effect of it on intubating conditions and onset time of intubation with respect to rocuronium as bolus.

MATERIAL AND METHODS

Present study was single-center, prospective, randomized study, conducted in department of anaesthesiology at XXX medical college and hospital, XXX, India. Study duration was of 1 year (July 2018 to June 2019). Study was approved by institutional ethical committee.

Inclusion criteria: Patients of age groups from 18-60 years of either sex, 40-60 kgs weight, ASA grades I and II, undergoing surgeries under general anaesthesia and given valid written consent for participation.

Exclusion criteria: Patients with neuromuscular diseases. Patients with anticipated difficult intubation. Patients with hepatic and renal diseases. Patients with history of any drug allergy. Pregnant female

Each patient was visited pre-operatively and counselled. Procedure was explained and Written, informed and valid consent was obtained from each patient.

The patients were randomly allocated into 2 groups of 30 patients each:

1. GROUP C (CONTROL group) - Patients have received 2ml of Normal saline as placebo and then intubating dose of inj. Rocuronium.
2. GROUP P (PRIMING group) - Patients have received 2ml quantity of PRIMING dose and then remaining intubating dose of inj. Rocuronium.

On arrival in the operation room, baseline parameters viz. heart rate, non-invasive mean arterial blood pressure, oxygen saturation were noted. A 20G cannula was inserted into a vein on the dorsum of patient's

non-dominant hand. Additional 20 G cannula on other hand was also secured for infusion of lactated ringer's solution to prevent dilutional effect. After explaining about the nerve stimulation technique to the patient, premedication was done with intravenous inj. Glycopyrrolate 0.004 mg/kg, and inj. Midazolam 0.02 mg/kg to all patients in both groups. Preoxygenation was started on venti-mask and after 10 minutes, priming dose/placebo as per group was given. Meanwhile supramaximal stimulus was fixed using NMT module in the Datex-Ohmeda, S/5 Avance machine. Total intubating dose of inj. Rocuronium bromide 0.6 mg/kg was diluted to 5 ml with normal saline. Drugs were loaded and administered by another experienced anaesthesiologist. The intubating anaesthesiologist was blinded to the study and diluting protocols. After pre-oxygenation, the priming dose of Rocuronium bromide 0.06 mg/kg²(10% of intubating dose) or normal saline was given i.v., 3 minutes before the intubating dose as per randomization. Fentanyl 2mcg/kg body weight was given intravenous 1 minute after the priming dose. Two and half minutes after giving the priming dose, patients were induced with intravenous Propofol 2 mg/kg body weight. Then the intubating dose of Rocuronium bromide was injected intravenous 3 minutes after priming or normal saline, as per randomization. After giving it, a supramaximally set Train Of Four (TOF) stimuli was applied through surface electrodes over the Ulnar nerve at the wrist. The stimulus was repeated after every 10 seconds and visually assessed for disappearance of T1 of TOF stimuli and loss of adduction of thumb.

ONSET TIME OF INTUBATION (OTI): the time interval between the intubating dose and the disappearance of T1 of TOF. Using the Cooper's scoring system, the intubating conditions were graded as excellent when intubating scores were between 8 and 9, good with 6-7, fair with 3-5 and poor with 0-2.

Table 1: Cooper's scoring system

Rate	Jaw relaxation	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 movement
3	Good (easy)	Open	None

All patients were monitored using electrocardiogram, non-invasive blood pressure and oxygen saturation with pulse-oximetry. Data noted included heart rate, mean arterial blood pressure, oxygen saturation with pulse oximetry, Cooper's score⁷ indicating about the intubation conditions and onset time of intubation. The above data were recorded at baseline, at induction, at intubation, 1 min and 5 min after endotracheal intubation. Descriptive statistics for the

continuous variables such as age, weight, heart rate, mean arterial pressure and SpO₂ and onset time of intubation were presented as mean and standard deviation while the inferential statistics for testing the hypothesis were performed with the unpaired “*t*” test. Categorical data like

sex, ASA grade were compared using the Chi-square test. Graphical representation was presented by bar diagrams and statistical analysis was performed using SPSS 20.0 (SPSS Inc. Chicago, IL, USA) statistical package. Statistical significance was considered if value of $P < 0.05$.

RESULTS

Overall, 60 patients were studied in age group of 18 to 60 years, 30 patients in each group C and group P. we compared mean age, weight, gender and ASA grade between group C and group P and difference was statistically not significant ($P > 0.05$).

Table 2: Comparison baseline characteristics between group C and group P:

Baseline characteristics	Mean \pm SD / no. of cases (%)		P value
	GROUP C	GROUP P	
Age (in years)	38.2 \pm 12.76	37.4 \pm 10.81	.79
Weight (kgs)	55 \pm 4.8	56.17 \pm 3.64	.29
Gender			
Male	17 (56.67%)	16 (53.33 %)	0.80
Female	13 (43.33%)	14 (46.67%)	
ASA grade			
1	26	27	.69
2	4	3	

We compared preoperatively baseline mean HR, mean HR at induction, mean HR at intubation, at 1 minute after intubation and at 5 minute after intubation between group C and group P, the difference between two groups was statistically insignificant. ($P > 0.05$).

Table 3: comparison of mean heart rate (HR):

MEAN HR	GROUP C	GROUP P	P VALUE
	Mean \pm SD	Mean \pm SD	
Baseline	74.8 \pm 9.7	76.37 \pm 6.6	0.47
Induction	71.4 \pm 8.2	74.97 \pm 6.8	0.73
Intubation	91.7 \pm 8.3	88.7 \pm 6.2	0.12
1 min	82.1 \pm 7.9	80.27 \pm 5.6	0.3
5 mins	72.9 \pm 7.2	73.43 \pm 5	0.72

We compared mean MAP preoperatively baseline, at induction, at intubation, mean HR at 1 minute after intubation and mean HR at 5 minute after intubation between group C and group P, the difference between two groups was statistically insignificant. ($P > 0.05$).

Table 4: comparison on basis of mean MAP

Mean MAP	GROUP C	GROUP P	P VALUE
	Mean \pm SD	Mean \pm SD	
Baseline	70.67 \pm 7.150	67.23 \pm 6.511	.06
Induction	70.53 \pm 6.967	68.80 \pm 6.316	0.73
Intubation	82.63 \pm 7.161	79.50 \pm 7.785	.32
1 min	76.83 \pm 5.414	73.93 \pm 6.486	0.3
5 mins	71.27 \pm 4.631	69.37 \pm 5.623	.11

We compared mean SPO₂ preoperatively baseline, at induction, at intubation, mean HR at 1 minute after intubation and mean HR at 5 minute after intubation between group C and group P, the difference between two groups was statistically insignificant. ($P > 0.05$).

Table 5: Comparison on basis of mean saturation (SPO₂)

Mean SPO ₂	GROUP C	GROUP P	P VALUE
	Mean \pm SD	Mean \pm SD	
Baseline	99.03 \pm 1.377	99.27 \pm 0.980	0.45
Induction	99.53 \pm 0.819	99.80 \pm 0.551	0.73
Intubation	99.13 \pm 1.332	99.40 \pm 0.932	0.15
1 min	99.57 \pm 0.728	99.57 \pm 0.858	0.3
5 mins	99.73 \pm 0.583	99.83 \pm 0.461	0.37

In group C, out of 30 patients, 17 patients were having score 9 while 12 patients were having score 8, while 1 patient had score 7 which was comparable with the group P in which out of 30 patients, 18 were having score 9, while 11 patients were

having score 8 and 1 patient was of score 7, so in both groups most of the patients (96.67% in each group) had excellent intubating condition, and the groups were comparable as statistically no significant difference was found after applying Independent samples Mann-Whitney U test with the P value of .804.

Table 6: Comparison on basis of Cooper's score

Cooper's Score	GROUP C	GROUP P	P VALUE
7	1	1	0.804
8	12	11	(Not significant)
9	17	18	

In group C mean Onset Time of Intubation was 92.33± 6.26 seconds, while in group P it was 56± 6.75 seconds, so the difference between the groups on the basis of OTI was statistically highly significant. (P value 0.0001)

Table 7: Onset time of intubation (OTI)

	GROUP C	GROUP P	P VALUE
	Mean ± SD	Mean ± SD	
Onset time of intubation	92.33 ± 6.26	56.00 ± 6.75	0.001

DISCUSSION

General anaesthesia is an important modality of anaesthesia since last many years. Routinely it takes some time for induction and intubation around 3-4 minutes. Under some circumstances there is a need for fast induction and intubation like trauma patients, pregnant females in fetal distress and many others. In such conditions Sch is the gold standard as it has very short onset of time. But it is associated with certain side effects because of which it is contraindicated in certain conditions like burn, head trauma etc., for which various non-depolarizing drugs has been tried. Among all these non-depolarizing neuromuscular blockers, rocuronium is found to be fastest, which with the help of PRIMING technique, can produce good intubating conditions in comparable time to as that of Sch. So rocuronium with priming could be an alternative to succinylcholine. Cooper *et al.*,⁸ found clinically acceptable intubating conditions and the mean onset time of intubation with 0.6 mg/kg rocuronium was 89 sec while with Sch 1 mg/kg it was 60 sec. McCourt *et al.*,⁹ found excellent intubating conditions at 60 s with succinylcholine 1 mg/kg and higher dose of rocuronium which was 1 mg/kg. Singh *et al.*,¹⁰ had shown that with 0.6 mg/kg rocuronium and 1.5 mg/kg succinylcholine, the time to achieve maximum blockade was 87.94 and 65.59 s, respectively. The intubating conditions were comparable in the two groups at 60 sec. Above studies shows rocuronium can be used as an alternative to succinylcholine. Naguib *et al.*,¹¹ had given the priming dose as 0.06 mg/kg rocuronium or 0.015 mg/kg mivacurium followed by an intubating dose of 0.54 mg/kg of rocuronium. On priming with rocuronium and mivacurium, the onset times were 73 and 58 s, respectively. In the other group, 1 mg/kg succinylcholine was administered and the onset time was found to be 54 s. Intubating conditions were similar in all three groups. It was concluded that priming rocuronium with either rocuronium or mivacurium resulted in neuromuscular

blockade comparable to that of succinylcholine in both the onset of action and intubating conditions. Griffith *et al.*,¹² compared priming with non-priming by giving a priming dose of 0.06 mg/kg rocuronium followed 2 min later by 0.54 mg/kg rocuronium and another group given directly 0.6 mg/kg rocuronium. Onset times were compared, which were 34±6 s with priming and 59±14 s without priming. Yavascaoglu *et al.*,¹³ also conducted a similar study and proved that priming with the 3 minutes priming interval irrespective of dose was more effective than the 2 min priming interval when rapid tracheal intubation with rocuronium was necessary. Taboada JA *et al.*,¹⁴ found that the priming interval of 4 min allowed the fastest onset time compared with the 2 and 6 min priming intervals. With the help of above studies rocuronium with priming may be used as an alternative to Sch. The autonomic safety ratio of rocuronium for vagal block is about 10-times less than that of vecuronium. No haemodynamic changes (blood pressure, heart rate) were seen in humans, and there was no increase in plasma histamine concentrations after doses of up to four-times ED95. Slight to moderate increase in heart rate may be due to either the fact that rocuronium produces pain on injection or to its weak vagolytic effect. The heart rate increase may be controlled by the prior administration of fentanyl.¹⁵ Shorten *et al.*,¹⁶ compared elderly patients given rocuronium 0.9 mg/kg with patients given vecuronium 0.12 mg/kg, and found no significant change in heart rate, arterial blood pressure or plasma epinephrine concentrations in either group. In present study, using the 2 × ED95 dose of rocuronium showed that with priming (priming with 10% of the intubating dose with 3-min priming interval), the onset time of intubation (onset of maximum block) was 56.00±6.75 s in the priming group and 92.33±6.26 s in the control group with clinically acceptable comparable intubating conditions in both groups at the time of intubation, i.e. after loss of T1 of TOF. This proves priming hastens the onset time of intubation significantly which is supported by the studies

done by Naguib *et al.*,¹¹ Griffith *et al.*,¹² Yavascaoglu *et al.*,¹³ and Taboada JA *et al.*,¹⁴ Priming dose can be associated with few adverse effects such as dysphagia, weakness, diplopia, breathing difficulties and generalized discomfort. Aziz *et al.*,¹⁷ explained the effects of priming with vecuronium and rocuronium in younger and elderly patients. In his study total number of patients was 10 in each group in young and elderly in both rocuronium and vecuronium groups. In younger patients, 7 in vecuronium and 6 in rocuronium developed ptosis, 5 in vecuronium and 4 in rocuronium developed difficulty in swallowing, expiratory reserve volume reduced by 20–25%, O₂ saturation was decreased but decrease was minimal in younger patients compared with the elderly. In elderly patients, 8 in vecuronium and 7 in rocuronium developed ptosis, 5 in vecuronium and 4 in rocuronium developed difficulty in swallowing, expiratory reserve volume reduced by 30–40%, O₂ saturation was decreased but decrease was higher in elderly patients than in younger patients. In present study none of the patients had evidence of such adverse effects of priming. The subtle symptoms of adverse effect of priming could not have been felt due to the administration of midazolam 10 min prior to the priming dose and use of fentanyl 2 microgram/kg 1 min after the priming dose. Thus priming dose of rocuronium is advantageous in patients for providing better quality of intubation with faster onset of action and in scenarios where fast intubation is needed and contraindication of succinylcholine exist, due to its own adverse effects, rocuronium with priming principle can be safely used. Therefore, rocuronium with priming principle can be a good alternative to succinylcholine for rapid sequence intubation.

CONCLUSION

Rocuronium with priming would be an excellent alternative to succinylcholine, whenever fast induction will be needed. Intubating conditions were good to excellent and comparable in both rocuronium with priming and without priming. NMT monitoring is a useful tool for indicating the clinically acceptable paralysis.

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