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Research Article

Efficacy study on intubating conditions at two different time intervals following rocuronium priming dose in major surgeries: A quasi randomized controlled study

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Abstract

Aims and Objectives: To compare the effects of two different priming intervals with the standard intubating dose of rocuronium on the onset time and intubation conditions.

Material and Methods: 40 patients were randomly assigned to two groups. Both the Groups were premedicated in usual manner. All the patients were induced with Thiopentone (5-7 mg/kg) after 2 minutes of priming dose (0.06 mg/kg) in Group R_2 and after 3 minutes of priming dose (0.06 mg/ kg) in Group R_3, till the loss of eye reflexes and then received intubating dose of injection Rocuronium (0.54 mg/kg).IPPR was given with 100% O_2 on bag and mask by circuit, intubated with direct laryngoscopy and maintained with O_2, N_2O, isoflurane and Atracurium/Vecuronium. Patients were reversed and extubated with full recovery.

Result and Summary: Clinically acceptable intubation conditions were obtained in all patients. 3 mins priming interval provides better and faster intubating conditions in Rocuronium as compared to 2 mins.

Conclusion: 3 min priming interval with rocuronium is better than 2 mins in terms of time of intubation and intubating conditions.

Keywords: Rocuronium, priming priniciple, intubating conditions

1. Introduction

Standard anesthetic technique used for patients, considered to be at risk of aspiration is known as rapid sequence induction (RSI). In order to prevent aspiration, the time between induction of anesthesia and intubation of the trachea should be kept as short as possible.

Succinylcholine is the most frequently used neuromuscular blocking agent for RSI because of its fast onset and fast recovery, despite of known side effects[1]. When succinylcholine is contraindicated, Rocuronium is an agent of choice with a fast onset and intermediate duration as compared to any other non-depolarising muscle relaxant[2].

The priming principle allows to shorten the onset time of a non-depolarizing muscle relaxant (NDMR) without increasing the duration of action by the application of a small subparalysing dose two to six minutes prior to the larger intubation dose.[3,4]

Priming dose of a NDMR should not cause unpleasant symptoms, but it should occupy a considerable portion of the post synaptic nicotinic acetylcholine receptors and shorten the onset time after administration of the intubation dose[5,6].

We compared intubating conditions at two different time intervals following rocuronium priming dose in major surgeries. The aim of the study was to evaluate the development of clinically acceptable tracheal intubating conditions and to compare the onset of neuro muscular blockade.

2. Materials and Methods

After obtaining approval of the institute's ethics committee and written informed consent from patients, the study were conducted in 40 patients of both sexes, age group of 20-60 years, ASA I & II, Modified Mallampati class I & II, admitted for various elective surgery in SBKSMIRC, Piparia.

Exclusion Criteria:

- Patients with acute cardiovascular, respiratory and renal disease
- History of drug sensitivity
- Patients on medication which interact with muscle relaxants, pacemaker, chemotherapy.
- All patients with neuromuscular disease.
- Obese patients(body mass index > 27)

Patient were kept nil by mouth overnight and after arrival of the patient in preoperative room, peripheral venous line was secured with 18 G vein flow in all patients through which inj. Ringer lactate or injection Dextrose Normal Saline was given. Premedicated with inj. Glycopyrrolate (0.2mg.), inj. Ondansetron (4 mg), inj. Midazolam (1 mg.) and inj. Tramadol (50-100 mg.). Acceleration transducer (TOF- Watch) was connected to the thumb and the electrodes were placed over the ulnar nerve on the medial side of the wrist and supramaximal stimulus was noted.[2]. All the patients were pre-oxygenated with 100% oxygen for 5- 10 minutes and priming dose of Rocuronium (0.06 mg/kg) was given. They were randomized in two groups, Group R_2 and Group R_3 based on quasi-randomization. Both the Groups were induce with Thiopentone (5-7 mg/kg) after 2 minutes of priming dose in Group R_2 and after 3 minutes of priming dose in Group R_3, till the loss of eyelash reflexes. After that all the patients will receive intubating dose of injection Rocuronium (0.54 mg/kg)[6]. All the drugs were given into rapidly running infusion of Ringer Lactate or Dextrose normal saline. IPPR with 100% O_2 on bag and mask by bain circuit and intubated with direct laryngoscopy.

Data of group R_2 and group R_3 were collected in prescribed forms containing patients' particulars and pre-induction variables -Pulse, Blood pressure, SpO2- before priming and after priming in Group R_2 and Group R_3 - Pulse, Blood pressure, SpO_2,visual disturbance, feeling of dyspnoea, difficulty in swallowing and TOF watch. After giving the intubating dose of rocuronium, a supramaximally set Train of Four (TOF) stimuli was applied over the ulnar nerve at the wrist through surface electrodes and was repeated every 10 s and assessed visually, for loss of adduction of thumb and disappearance of T1 of TOF stimuli. Time interval between the intubating dose and the loss of T1 of TOF stimuli as measured by stopwatch was considered as "onset time of

intubation". After loss of T1 of TOF stimuli, the trachea was intubated in sniffing position and intubating conditions were noted. Intubation score recorded using an intubation scoring system and 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 (Cooper *et al.*)[7].

Intubation time will recorded as the number of seconds from the end of administration of intubating dose of relaxant to the loss of T1 of TOF stimuli, as measured by a stop-watch. Vital parameters like blood pressure, electrocardiogram, SpO_2 and neuromuscular twitches using peripheral nerve stimulator will be monitored intraoperativaly in both groups. Post-induction variables same as pre induction variables were monitored.

Patient was maintained on O_2, N_2O, isoflurane and muscle relaxant. Patient will be extubated after end of surgery and vital parameters were monitored and recorded.

3. Results

Table 1: Showing the distribution of demographic characteristics among the two groups

	R_2		R_3		'P' Value
	Mean	SD	Mean	SD	
Age	31.95	4.8	31.4	31.4	0..756
Weight	54.05	8.18	51.4	51.4	0.285
Sex	8/12			9/11	

Table 2: Showing haemodynamic state after priming in both the Groups

	R_2		R_3		'P' Value
	Mean	SD	Mean	SD	
HR	91.2	15.12	98.9	17.62	0.18
SBP	128.85	12.2	129.35	15.03	0.93
DBP	85.1	7.57	81	10.97	0.22
SPO_2	100	0	100	0	

Figure 1: Showing timing of intubation

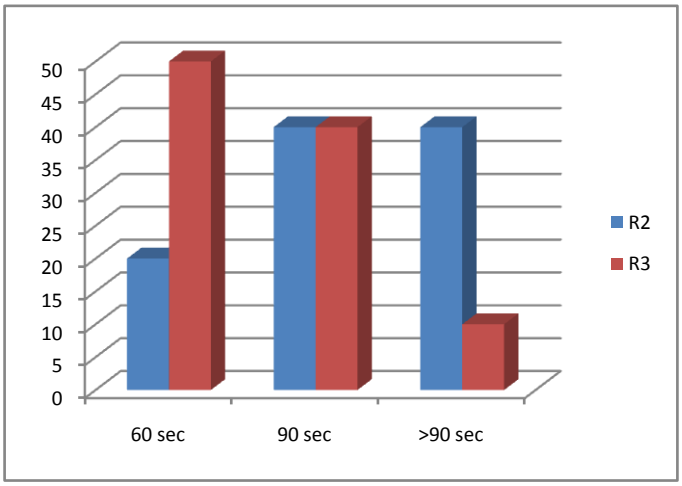

Figure 1 shows that 20% patients of group R_2 and 50% patients in group R_3 were intubated with in 30 seconds. Timing of intubation were significantly faster in Group R_3 (P value = 0.006)

Table 3: showing Comparison of jaw relaxation among both groups

	R_2	R_3	'P' Value
Minimal	2 (10%)	0	0.09 (λ^2 test)
Moderate	8 (40%)	4 (20%)	
Good	10 (50%)	16 (80%)	

Table 4: showing response to intubation among the groups.

	R_2	R_3	'P' Value
Mild Cough	0	0	0.015 (λ^2 test)
Slight diaphragmatic movement	10 (50%)	2 (10%)	
None	10 (50%)	18 (90%)	

Table 5: showing position of vocal cords in both groups

	R_2	R_3	'P' Value
Closing	0	0	0.341
Moving	4 (20%)	1 (5%)	
Open	16 (80)	19 (95%)	

Table 6: showing total intubation score in both groups

	R_2	R_3	'P' Value
0 – 2	0	0	0.026
3 – 5	2	0	
6 – 7	8	2	
8 - 9	10	18	

4. Discussion

Various techniques have been used to reduce intubation time of non-depolarizing NMBA like (1) timing principles, (2) high dose of non-depolarizing muscle relaxants, (3) inhalational agents to augment the effect of non-depolarizing muscle relaxants, (4) use of intravenous anaesthetic agents with non-depolarizing muscle relaxants to augment neuromuscular blockade and (5) priming principle.[8]

In our study, we have used the priming principle which is a divided dose technique of neuromuscular blocking drug, capable of producing a rapid onset of neuromuscular block and suitable intubating condition. A small priming dose (10% of intubating dose) 3 minutes prior to induction is administrated to an awake patient. This dose is large enough to cause moderate inhibition of neuromuscular transmission but small enough to cause any unpleasant side effects. It occupies 75% of end plate receptors. After 2–3 min, the rest of the intubating dose of the drug is administered to produce neuromuscular blockade for rapid sequence intubation. A suitable priming dose would allow patients to maintain adequate respiration, protect his airway and be well tolerated.[9]

Priming technique with Rocuronium has been investigated by several authors but studies comparing priming principle with two different time interval have not been done extensively in an attempt to reduce the intubating time and also to optimize its efficacy and reduce the incidence of side-effects.

The present study was undertaken to compare the time of intubation and intubating conditions using priming principle with two different priming intervals with Rocuronium.

There were no statistically significant differences in distribution of age, sex and weight between both groups. ($P > 0.05$) (Table 1)

Priming principle was used by various authors like Shashank *et al*[10], Griffith *et al*[6] with priming interval of 2 minutes; Rao *et al*[8], Md. Liaquatunnoor[11] with 3 minute priming interval and Yavascaouglu *et al*[12] has compare two different priming interval of 2 minutes and 3 minutes.

Table 7: Showing time of intubation with 2 min and 3 min priming interval

Authors	2 min	3 min
Naguib *et al*	-	73 sec (57-90)
Md. Liaquatunnoor	-	<60 sec in 86.7 %
Rao *et al*	-	50.67 ± 7.39 sec
Yavascaoglu *et al*	79.5 ± 22.4 sec	63.2 ± 18.6 sec
Griffith *et al*	34 ± 6 sec	-
In our study	77.4 sec	64.6

4(20%) patients of group R_2 and 10(50%) patients of group R_3 were intubated within 60 seconds (77.4 second in group R_2 and 57.13 second in group R_3 respectively). 8(40%) patients of group R_2 and 2(10%) patients of group R_3 have taken >90 seconds for intubation (93.4 seconds in group R_2 and 94.7 seconds in group R_3). Group R_3 allowed earlier intubation compared to group R_2. (p value- 0.006- highly significant).

Griffith *et al*.[6] used a priming dose of 0.06 mg/kg and after priming interval of 2 minutes, intubating dose of 0.54 mg/kg were administered to compare onset times and intubating conditions with the patients receiving rocuronium 0.6 mg/kg in bolus dose. They found that the onset times with rocuronium priming was 34±6sec. His finding didn't match with our findings, this may be due to use of propofol - fentanyl for induction.

Yavascaoglu *et al*.[12] studied 75 adult patients (17– 67yr.) using different priming interval (two and three minutes) and priming doses (priming dose: rocuronium 0.06 or 0.1 mg/kg, intubating dose 0.54 or 0.5 mg/kg). They found that priming with three minutes interval shortened the onset time of rocuronium, while a two-minute interval did not significantly decrease the onset time. This finding is comparable to our study.

Naguib[13] studied 70 patients divided equally in 7 groups and compare different priming combinations and reported significant acceleration of the onset times of rocuronium in the priming group using same priming dose and 3 min priming interval. They found that the onset times with rocuronium priming was average 73 seconds. However, he administered additional thiopental sodium 2 mg/kg immediately prior to tracheal intubation. This difference in onset time of intubation may be due to small sample size.

Rao *et al*.[8] studied 60 patients to compare onset time of intubation and its condition with Rocuronium with and without priming principle and found that onset time was 50.67 seconds with priming. This study also favours our finding.

In our study 10 (50%) patients of Group R_2 and 16 (80%) of Group R_3 exhibited good relaxation of jaw at the time of intubation. The moderate relaxations were achieved in 8(40%) and 4(20%) patients in Group R_2 and Group R_3 respectively. Jaw relaxation was better in group R_3 (p - 0.09 – Highly Significant)

One study done by Liaquatunnoor *et al*[11] achieved good jaw relaxation in 18 (60%) patients and moderate relaxation in rest of the patients. He has used Rocuronium in dose same as done by us using priming technique with 3 min priming interval.

16 (80%) of Group R_2 and 19 (95%) of Group R_3 showed completely open vocal cord for successful intubation. However this difference was not significant (P value – 0.341). Liaquatunnoor *et al*[11] also achieved open vocal cords in 20 (66.7%) patients by using 3 minutes priming interval.

In terms of response to intubation R_3 group was better than group R_2. 18 (90 %) of Group R_3 showed no response at all to intubation. 2 (10%) of Group R_2 and 10 (70 %) of Group R_3 responded to intubation by slight diaphragmatic movement. Smooth intubation was better in Group R_3 compared to group R_2 (p = 0.015 – Significant). But Liaquatunnoor *et al*[11] has done the study which shows slight diaphragmatic movement in 20 (66.7%) patients in 3 minute priming interval. Surprisingly it was more than seen in our study.

The intubating conditions achieved with priming interval of 2 minutes by shsashank *et al*[15] and present study is shown below.

Table 8: intubating conditions achieved with priming interval of 2 minutes

Authors	Excellent	Good	Fair	Poor
Shashank *et al*	30 (85.71%)	4 (11.42%)	1 (2.85%)	0
In our study	15(50%)	12 (40%)	3 (10%)	0

The intubating conditions achieved with priming interval of 3 minutes by various authors and present study is shown below.

Table 9: intubating conditions achieved with priming interval of 3 minutes

Authors	Excellent	Good	Fair	Poor
Naguib *et al*	6 (60%)	4 (40%)	0	0
Md. Liaquatunnoor	16 (53.3%)	14 (46.7%)	0	0
In our study	27 (90%)	3 (10%)	0	0

Based on intubation score 10 (50 %) of Group R_2 and 18 (90 %) of Group R_3 were categorized as having excellent intubating conditions. The rest of the patients, in both the groups, except 2(10 %) patients of Group R_2, had good outcome. The mean intubation score in both groups were statistically highly significant (p = 0.026 – Significant.)

In our study there were rise in all hemodynamic parameters during intubation. Increase in pulse rate was 41.75% in group R_2 and 54.91% in group R_3 at intubation and returned to base line value at 20 minutes in group R_2 and at 30 minute in group R_3. SBP and DBP were rise up to 22.02% and 22.3% respectively in group R_2. It took 10 minutes for returning to baseline value. Not significant. Similarly in group R_3 there were also rise in SBP and DBP which was 20.88% and 25.95% respectively, it took 15 minutes for returning to baseline value.

In this study, only 1 patient in group R_2 and 3 patients in group R_3 had SBP >150 mmhg after priming. (151 mmhg in group R_2 and 157.66 mmhg

in group R_3). Importantly during intubation, SBP was more stable in group R_3 (161.33 mmhg) as evident by only 15(50%) patient experienced SBP more than 150 mmhg compared to 19 (63.33%) patients in group R_2(162.57 mmhg). No treatment was required for that and all parameters came to baseline value after 10-15 minutes. However these may be due to use of xylocaine – adrenaline infiltration by surgeons in all patients.

In our study, 1 (5 %) patients in group R_3 and 1 (5 %) in group R_2 experience feeling of dyspnoea, however they were effectively managed by IPPR by bag, mask and Bain circuit, than patient was induced. There was no bronchospasm or rash associated with fall in blood pressure. No other patients in the both groups had any clinical evidence of histamine release. This concurs with study of Levy *et al*.[14]

5. Conclusion

From the above description, it is clear that for faster acting non-depolarizing NMBA, like rocuronium, using 'priming principle' has significant beneficial effects on reducing the onset time and ensuring better intubating conditions. Very less clinically significant side effects were observed due to priming in our study. In the result of this study, we also observed that 3 min priming interval allowed much earlier intubating conditions compared to 2 min. So, rocuronium 0.6 mg/kg total dose with 3 min priming interval following induction with thiopental sodium can be a suitable alternative to suxamethonium for rapid tracheal intubation for surgical procedures of short and medium duration.

References

1. Sparr HJ. Choice of the muscle relaxant for rapidsequence induction. *Eur J Anaesthesiol* 2001; 18(Suppl. 23): 71–6.
2. Wierda JM, Hommes FD, Nap HJ, van den Broek L. Time course of action and intubating conditions following vecuronium, rocuronium and mivacurium. *Anaesthesia* 1995; 50: 393–6.
3. Hofmockel R, Benad G, Kabott A. Mechanomyographic and electromyographic studies of endotracheal intubation with 2 different rocuronium dosages. *Anaesthesiol Reanim* 1994; 19: 144–8.
4. Foldes FF, Nagashima H, Kornak PH. Effect of priming. *Anaesth Pharmacol Rev* 1993; 1: 49–56.
5. MiIIer RD. The priming principle (Editorial). *Anesthesiology* 1985; 62: 381–2.
6. Griffith KE, Joshi GP, Whitman PF, Garg SA. Priming with rocuronium accelerates the onset of neuromuscular blockade. *J Clin Anesth* 1997; 9: 204–7.
7. Cooper RA, Mirakhur RK, Maddineni VR: Neuromuscular effects of Rocuronium bromide during fentanyl and halothane anaesthesia, *Anaesthesia*, 1993; 48:103-105.
8. Rao Hanumantha M *et al*, Comparison of intubating conditions between rocuronium with priming and without priming: Randomized and double-blind study, *Indian Journal of Anaesthesia*, 2011; 55, 5, 494- 498.
9. Foldes F. Rapid tracheal intubation with nondepolarizing neuromuscular blocking drugs: the priming principle (Letter). *Br J Anaesth* 1984; 56:663
10. Shashank DS, Singh N Ratan, Singh L Kameshwar. Effects of pretreatment with different neuromuscular blocking agents on facilitation of intubation with rocuronium: A prospective randomized comparative study; *Indian Journal of Anaesthesia*, 2014; 58(3); 303-308.
11. Md. Liaquatunnoor, Rubina Yasmin, UH Shahera. A study of priming technique of Rocuronium in facilitating intubation, *Journal of BSA*, 2008; 21 (1):3-11.
12. Yavascaoglu, B, Cebelli, V, Kelebek, N, Uçkunkaya, N, Kutlay, O. Comparison of different priming techniques on the onset time and intubating conditions of rocuronium; *European Journal of Anaesthesiology*. 2002; 19(7):517-521.
13. Naguib M, Samarkandi AH, Ammar A and Turkistani A: Comparison of suxamethonium and different combinations of rocuronium and mivacurium for rapid tracheal intubation in children; *British Journal of Anaesthesia*, 1997; 79: 450-455.
14. Levy JH, Davis GK, Duggan J, Szlam F: Determination of the hemodynamics and histamine release of rocuronium (Org 9426) when administered in increased doses under N_2O/O_2-sufentanil anesthesia, *Anesth Analg*. 1994 Feb; 78(2):318-21.
15. Shashank DS, Singh N Ratan, Singh L Kameshwar. Effects of pretreatment with different neuromuscular blocking agents on facilitation of intubation with rocuronium: A prospective randomized comparative study; *Indian Journal of Anaesthesia*, 2014; 58(3); 303-308.