

Randomized Single Blinded Comparative Study on Intubating Conditions of Rocuronium with and Without Priming

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Abstract: Background: Rocuronium with priming may produce comparable intubating time and conditions to that of succinylcholine. Rocuronium with priming may be an alternative to succinylcholine in rapid sequence intubation in conditions where succinylcholine is contraindicated. The present study is conducted to compare the intubating conditions and the intubation time of Rocuronium with and without priming.

Methods: A randomized single blinded control study done in one hundred patients of ASA Physical Status of I and 2, aged between 18 & 65 years, of both sex, were divided into priming and control groups of 50 each. Patients in the priming group received 0.06 mg/kg of Rocuronium, those in control group received normal saline. All patients received fentanyl 1 mcg/kg followed by Thiopentone 5mg/kg for induction. Intubating dose of Rocuronium 0.54mg/kg in the priming group and 0.6mg/kg in the control group were administered 3 min after priming. Onset time of intubation was assessed using Train of Four stimuli, and the intubating conditions were compared by the Cooper scoring system.

Results: The onset time of intubation is 59.45 +/- 0.73 seconds in the priming group and 69.97 +/- 2.72 seconds in the control group, with the excellent intubating conditions in both the groups and without any adverse effects.

Conclusion: Priming with Rocuronium provides excellent intubating conditions within 60 seconds with no adverse effects.

Key Words:- Rocuronium, Priming, TOF.

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I. Introduction

Rapid and safe endotracheal intubation is of paramount importance in general anaesthesia. Rapid sequence induction and endotracheal intubation using Succinylcholine is an established technique in patients at risk of gastric aspiration. But, Succinylcholine has a number of undesirable side effects like muscle fasciculation, myalgia, hyperkalaemia⁽¹⁾, bradyarrhythmias⁽²⁾, increased intra-ocular tension, increased intracranial tension⁽³⁾, increased intra gastric pressure, anaphylaxis, malignant hyperthermia and masseter spasm. Hence, it is not suitable in situations like neuromuscular disorders, burns, acute head injury, intracranial bleed⁽⁴⁾, open eye injury, spinal cord injury⁽⁵⁾, cerebrovascular accidents and renal diseases. The above side-effects and contraindications of Succinylcholine had prompted the use of non-depolarizing muscle relaxants.

Rocuronium bromide has the fastest onset time compared with other non-depolarising neuromuscular blocking drugs. It produces comparable intubating conditions to that of Succinylcholine, but does not have the short intubation time of the latter. Hence, it may not be preferable for rapid sequence intubation, but Rocuronium with priming may produce comparable intubating time and conditions to that of Succinylcholine.

In this study, we have used the priming principle in order to hasten the onset time and provide better intubating conditions. It is a divided dose technique of neuromuscular blocking drug, capable of producing a rapid onset of neuromuscular block and suitable intubation condition. A small priming dose (10% of intubating dose) is administered 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 like dyspnea, diplopia. It occupies 75% of end plate receptors. 2.5 mins later induction agents and 3 mins later the rest of the intubating dose of the muscle relaxant are administered to produce neuromuscular blockade for rapid sequence intubation⁽⁶⁾.

We chose Rocuronium bromide with an intubating dose of 0.6 mg/kg⁽⁷⁾, priming dose of 0.06 mg/kg⁽⁸⁾ (10% of intubating dose) and priming interval of 3 min⁽⁹⁾ for our study.

The present study is undertaken to evaluate the efficacy of the priming principle using Rocuronium bromide in reducing the onset time of intubating and also to evaluate the intubating conditions. So by using the

priming principle on Rocuronium bromide, the onset time of the neuromuscular bromide may be hastened as that of the Succinylcholine⁽¹⁰⁾ so that it can be used in rapid sequence intubation in conditions where contraindications for Succinylcholine exists.

Aim: To compare the intubating conditions and the onset time of intubation of Rocuronium with and without priming.

II. Materials And Methods

A Single blinded randomized control study was conducted in Department of Anaesthesiology Government medical college, Srikakulam during March 2018 to march 2019 after obtaining permission from institutional ethical committee and written and informed consent from patients. Patients posted for elective surgery under general anesthesia in supine or lithotomy position. Patients between 18 and 65 years, ASA PS 1 or 2 and cases Posted for elective surgeries under general anesthesia were included in the study. Patient with neuromuscular disease, anticipated difficult intubation, allergic to Rocuronium bromide and Patients on chronic medications which may interfere with Rocuronium action were excluded from study.

Sample Size was calculated based on study conducted by M Hanumantha Rao et al⁶, mean onset of time of intubation in non-priming group μ_1 was 94 seconds, priming group μ_2 was 50.67 seconds and corresponding standard deviations were 11.62(s1) and 7.39 (s2) with this data sample size to get 80% power and 95% confidence level the minimum sample size required was found to be 68 with 34 in each group. So we took sample size of 50 in each group considering dropouts.

Sampling method is convenience sampling and from the patients who are presenting the major operation theatre during the study period. Patients will be divided into two groups, one with priming Group assigned as 'P' and the other non-priming group assigned as control Group "C". Patients will be allocated in either group based on random numbers allotted to patients. Random numbers will be generated using random number generator.

It is a divided dose technique of neuro muscular blocking drug, capable of producing a rapid onset neuromuscular block and suitable intubation conditions. A priming dose [10% of total intubation dose] is administered 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 copies 75% of end plate receptors.

After 3 minutes, the rest of the intubating dose of the drug is administered to produce neuromuscular block for rapid sequence intubation. Rocuronium bromide has the fastest onset time when compared with the other no depolarizing muscle relaxants. We chose Rocuronium bromide with an intubating dose of 0.6mg/kg, priming dose of 0.06 mg/kg [10% of intubation dose] and priming interval of 3 min.

All the patients included in the study underwent a detailed pre anaesthetic checkup. Basic laboratory investigations such as haemoglobin, random blood sugar, serum creatinine and ECG were taken in all patients. The study drugs were prepared at operating room temperature by the investigator. Only the patient was blind regarding the contents of solution. Drugs and equipments necessary for resuscitation and general anaesthesia were kept ready.

All patients were kept NPO for atleast 8 hrs; In the operation theatre intra line was secured with 18G, monitors ECG, Sphygmomanometer, pulseoximeter were attached. Inj. Glycopyrolate 0.2mg iv and inj. midazolam 1 mg iv given to all patients in both groups 10 mins prior to the priming dose. Supra maximal stimulus was set with a peripheral nerve stimulator [PNS]. Total intubating dose of Rocuronium bromide 0.6mg/kg was diluted to 5 ml. In Group 'C' 2ml of normal saline was taken in a 2 ml syringe. In Group 'P' 0.5 ml of Rocuronium bromide from 5 ml was taken and diluted to 2ml with normal saline and the remaining 4.5ml was diluted to 5ml with normal saline. Drugs were loaded, labelled and administered by investigator.

After preoxygenation, the priming dose of Rocuronium bromide 0.06mg/kg [10% of intubating dose] or NS was given 3 min before as per randomization. The patients were enquired about the ptosis, double vision, difficulty in swallowing and difficulty in breathing. Inj fentanyl 1mcg/kg was given iv 1 min after the priming dose. 2.5 mins after giving the priming dose, patient was induced with inj thiopentone sodium 5mg/kg over 20 seconds. The intubating dose of Rocuronium was injected 3 min after the priming or NS injection.

After giving the intubating dose of Rocuronium bromide, a supramaximally set TOF stimuli were applied over ulnar nerve at the wrist through surface electrodes and was repeated every 10 seconds and usually assessed for loss of adduction of thumb and disappearance of T1 of TOF stimuli. The time interval between the injection of intubating dose and the loss of T1 response of TOF stimuli was considered as onset time of intubation. After loss of T1 of TOF stimuli, the trachea was intubated. All patients were monitored for heart rate, blood pressure and oxygen saturation. Tracheal intubation and grading of intubating conditions was performed by investigator. Intubating conditions were evaluated by Cooper et al intubation scoring system and graded as excellent if score was 8 & 9; good if score was 6 & 7; sir if score was 3 to 5; poor if score was between 0 to 2.

III. Statistical analysis

Descriptive statistics for continuous variables such as onset time of intubation were presented as mean and standard deviation while the inferential statistics for hypothesis testing were performed with the Unpaired "t" test. Graphical representation was presented by bar diagrams and statistical analysis was performed using SPSS 17.0, Statistical significance was considered if $P < 0.05$.

IV. Observation and results

Table 1. Comparison of Heart Rate (HR)

	Priming			Control		
	HR1	HR 2	HR 3	HR 1	HR 2	HR 3
Mean	75.1	76.46	76.68	79.91	84.07	84.58
STD DEV	14.10	13.96	11.90	17.93	10.56	10.13
MEDIAN	75	75	76	84	84	84
MIN	54	50	55	5	60	65
MAX	110	112	110	110	110	110
P Value		0.100	0.075		0.075	0.068

HR 1 - Baseline Heart rate

HR 2 – Heart rate at 1 min

HR 3 – Heart rate at 3 min

There was increase in Heart rate at 1 min and 3 min after intubation from the baseline value, but a statistically significant level was not attained.

Table 2. Comparison of Mean Arterial Pressure (MAP)

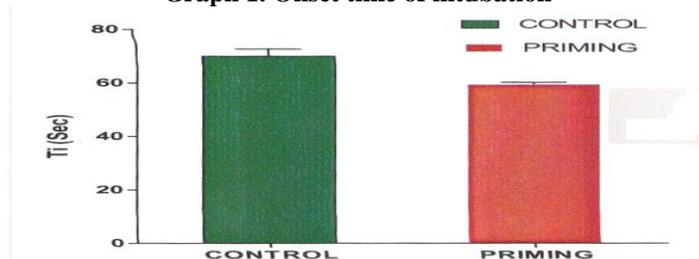
	Priming			Control		
	MAP 1	MAP 2	MAP 3	MAP 1	MAP 2	MAP 3
Mean	94.71	95.65	96.54	95.02	96.69	96.81
STD DEV	8.78	8.42	7.75	10.78	9.81	9.29
MEDIAN	96	97	98	96	98	98
MIN	73	73	82	72	73	73
MAX	111	113	115	122	117	113
P Value		0.280	0.599		0.090	0.058

There is no significant increase in mean arterial pressure.

Table 3. Onset time of intubation

Ti (sec)	Priming	Control	P Value
Mean	59.45	69.97	0.0001
S D	0.73	2.72	
Median	60	70	
Range	57-61	63-75	

Graph 1. Onset time of intubation



The time to loss of T1 of TOF was significantly shorter (59.45 ± 0.73) in priming group as compared to control group (69.97 ± 2.72).

According to Cooper et al scoring system the intubating condition was excellent (8-9) in 98.24% priming group and 90.69% of control group and was good (6-7) in 1.76% of priming group and 9.31% of control group.

V. Discussion

The study was done to compare the intubating conditions of Rocuronium with and without priming. In this present study, 100 ASA grade I and II patients of either sex and aged between 18 and 65 years were selected and randomized into two groups, the control group (normal saline and intubating dose or Rocuronium 0.6 mg/kg as intubating dose) and priming group (0.06 mg/kg of Rocuronium as priming dose and 0.54 mg/kg of Rocuronium as intubating dose).

The heart rate and mean arterial pressure were increased at 1 min and 3 min after intubation, but there was no significant change in HR, SBP, DBP and MAP after intubation in either of the groups in the study.

In these patients Rocuronium can be used safely as it does not cause bradycardia, rather, it causes slight tachycardia which is not significant clinically. As there is no significant change in HR and MAP with Rocuronium, it is the agent of choice in cardiac and other haemodynamically unstable patients.

In our study the mean onset time was 59.45 ± 0.73 seconds in priming group and 69.97 ± 2.72 seconds in control group.

In study Heier et al¹¹, Shorten et al¹² have advocated the use of higher dose of Rocuronium like 0.9 mg/kg or 1.2 mg/kg to reduce onset time but at the cost of unnecessarily prolonging the duration of action, which is not clinically acceptable in many situations. It is better to use Rocuronium in doses of 0.6 mg/kg with priming to reduce the onset time.

Griffith et al⁹ compared priming with non priming by giving a priming dose of 0.06 mg of rocuronium followed 2 min later by 0.54mg/kg rocuronium and in another group 0.6mg/kg rocuronium directly. Onset time were compared, which were 34 ± 6 s with priming and 59 ± 14 s without priming .

Jose et al¹³ found that the priming interval of 4 min allowed fastest onset time than 2 min and 6 min. Yavasscaoglu et al¹⁴ has proved that priming interval of 3 min is more effective than 2min or 4 min.

In the present study with priming interval of 3 min we found that all patients showed clinically acceptable intubating conditions with Rocuronium 0.6 mg/kg, being excellent in 98.24 % of priming group and 90.69 % of control group and good in 1.76 % of priming group and 9.31 % of control group. Rocuronium with priming may be an alternative to succinylcholine in rapid sequence intubation in conditions where succinylcholine is contraindicated.

Conclusion: Priming with Rocuronium provides excellent intubating conditions in less than 60 seconds with no adverse effects.

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