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Comparative study of intubating time and intubating condition using rocuronium with and without priming technique in patients undergoing elective surgeries under general anaesthesia: a double blinded, prospective and randomized control study

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ABSTRACT

Priming is a technique where NMB is provided in two divided doses to accelerate the onset of action. Compared to other non-depolarising neuromuscular blocking agents Rocuronium has faster neuromuscular blocking property and produces condition favourable for the intubation.

Objectives: 1) To compare the time of onset of neuromuscular blocking drug with priming principle using TOF monitor.2) To assess the condition during intubation based on Steyn's modification of Helbo-Hansen scoring system.
Methodology: A prospective Randomised controlled trial were conducted among 75 patients those who underwent elective surgery under general anaesthesia, was randomized into 3 groups. Group A as control group, where normal saline was given as priming dose followed by 0.6 mg/Kg of rocuronium. Group B and C received a priming dose of 0.06 mg/kg and 0.1 mg/kg with the intubating dose of 0.54 mg/kg and 0.5 mg/kg respectively. The outcomes that were studied include the onset time and intubating condition.
Results: The onset time was found to be least in group C followed by group B and group A. The difference was found to be statistically significant. The priming dose of 0.10 mg/Kg and intubating dose of 0.50 mg/Kg was found to have the rapid onset of action among the three and the intubating conditions were excellent in all 3 groups.
Conclusion: The priming dose of 0.10 mg/Kg of rocuronium in combination with its intubating dose of 0.5 mg/kg, had accelerated the time of onset of rocuronium. Intubating condition produced by rocuronium were excellent either with priming or not.

Endotracheal intubation involves introduction of endotracheal tube into the trachea in order to maintain a patent airway. To achieve excellent conditions for intubation without using muscle relaxants, generous doses of propofol and opioids are needed which in turn delays awakening and risks compromising the hemodynamic stability of the patient. Furthermore, intubation without using muscle relaxants is associated with an increased risk of laryngeal trauma. It also will aid in decreasing the risk of pulmonary aspiration. Most commonly an endotracheal intubation would be performed either for surgical procedures or at the time of emergencies[(1)]. Rapid sequence intubation (RSI) is done to support the process of endotracheal intubation in conditions of full stomach, inadequate NPO status, intestinal obstruction etc. In case of RSI there will be pre-treatment with paralytic medications. This pre-treatment improves the visualisation of larynx by diminishing various reflexes, thereby making endotracheal intubation easier[(2)]. While performing a rapid sequence induction of anaesthesia, the interval between the induction of anaesthesia and securing airway would be the crucial period. This time interval should be kept shortened as much as possible[(3)].

Neuromuscular blockade in case of RSI will be produced by the neuromuscular blocking agents that block the nicotine acetylcholine receptor (NAchR). Neuromuscular junction (NMJ) in the motor neurons of skeletal muscle

contains NAchR. This neuromuscular blockade aid in maintaining a patent airway along with respiratory management. They also enhance the surgical field conditions[4].

Succinylcholine is the agent of choice for producing neuromuscular blockade during surgeries due to its rapidly acting property and shorter duration of action. The problem with succinylcholine is the amount of side effects like it tends to produce like hyperkalemia, bradycardia, myalgia, increased intracranial pressure etc. A non- depolarizing neuromuscular blocking agent (NDNMB) would be relatively safer in terms of side effects produced[5]. Though NDNMB were safe, they did not have the desired property of action. Rocuronium matches the onset action of succinylcholine. But on the other side, it has a duration of action much more than that of succinylcholine[6].

To the question whether succinylcholine can be replaced by rocuronium, a consensus is yet to be achieved. In day to day practice rocuronium is often used in those circumstances where succinyl choline is contraindicated[7].

In order to optimise the usage of nondepolarizing neuromuscular blockers to aid in rapid sequence intubation, many techniques like timing principle, priming principle, muscle relaxant combination, higher dose of non-depolarizing muscle relaxants etc have been proposed[5]. Priming principle is one such technique. Here different doses of the neuromuscular blocking agents (NMBA's) are provided at varied time intervals. The initial dose provided is called 'the priming dose' and the one later will be 'the intubating dose.' The priming dose provided will be a sub paralysing dosage and will be almost ten percentage of the intubating dose[8]. This priming dose will produce moderate inhibition of the neuromuscular transmission but will not be producing any unpleasant side effects. The priming dose will also enable rapid reaching of the intubating dose to the Neuromuscular junction (NMJ)[9].

For each neuromuscular agent the priming dose, intubating dose, and the time interval between the two will not be similar and will be depending on various factors like the type of NMBA's and the total dose required to produce the desired effect. Various studies have been done with different non depolarizing NMB agents with their respective priming and intubating doses. For example, the priming dose of Vecuronium is 0.01mg/kg where as in Inj.Atracurium,0.05mg/kg is considered as priming dose [10]. In another study, various priming doses of rocuronium (0.06mg/kg and 0.01mg/kg) were compared at two different priming intervals, they found that regardless of priming doses, the time interval was more significant and added that greater the time interval, shorter the onset time of intubation.

Our current study was appraised to evaluate the efficacy of two different priming dose of rocuronium at 3 minutes interval in minimizing the onset time of intubation and improving the condition of intubation.

Materials and Methods

This prospective randomized controlled was performed on 75 patients admitted in tertiary care center, Chettinad Hospital and Research Institute under department of anaesthesiology. After obtaining approval from institutional ethical committee, 636/IHEC/12-19, the study was performed for patients undergoing planned surgeries under GA either gender aged between 18 and 65 years belonging to ASA I and II with BMI<30 kg/sq.m. Patients with anticipated difficult airway, neuromuscular diseases, liver, renal and neurological disorders and pregnant women were excluded from the study. Sample size was computed based on the study done by Hanumantharao et al.,2011, and was approximated to 25 in each group. Patients in Group A received 2ml of normal saline as priming dose followed by full intubation dose of rocuronium 0.6mg/kg in a 5ml syringe intravenously. Patients in Group B and C received a priming dose of 0.06 mg/kg and 0.1 mg/kg with the intubating dose of 0.54 mg/kg and 0.5 mg/kg respectively. All of them received the priming dose intravenously immediately after preoxygenation and the intubation dose in all the three groups was diluted to 5ml with normal saline in a 5ml syringe and was given intravenously 3 minutes after the priming dose.

All the patients underwent routine pre-operative assessment on the day before the surgery. Routine fasting guidelines were followed, six hours for soft diet and 4 hours for liquids prior to the surgery. The patients were pre-medicated with Tab.Ranitidine (150 mg) on the night prior to the surgery and at about 6 am on the day of surgery. Intravenous line was secured with 18 or 20G IV cannula and ringer lactate infusion was initiated.

Once the patient gets shifted to the operating room, basic vital monitors like pulse oximetry, Non-invasive Blood pressure (NIBP) and Electrocardiograph (ECG) were connected and recorded. After explaining the nerve stimulation procedure. neuromuscular monitor (TOF-Watch®SX, organon, ireland) was connected. Two electrodes and a temperature probe were placed on the volar aspect of the wrist so as to stimulate the ulnar nerve. Distal electrode(negative) was placed 1cm proximal to the proximal flexor crease of the wrist whereas the proximal electrode(positive) was connected 4-5cms proximal to the distal electrode. On electrical stimulation, finger flexion and thumb adduction were elicited. All the patients were pre-medicated with Inj.Glycopyrolate 0.2mg, Inj.Midazolam 1mg 30 minutes prior to the procedure. All patients were pre- oxygenated with 100% oxygen. After which the priming dose of the study drug was given 3minutes prior to the intubating dose

as per the study protocol and were assessed for any adverse effects like ptosis, double vision, difficulty in breathing and difficulty in swallowing. Inj.Fentanyl (2mcg/kg) was given intravenously, 1minute after the priming dose. Two minutes after the priming dose, patients were induced with Inj. Propofol (2mg/kg) over a period of 60 seconds. The intubating dose of rocuronium bromide was given after 3 minutes of priming dose or normal saline injection. The time at which the intubating dose was administered was noted(t1).

Following the intubating dose, a supramaximal Train of Four (TOF) stimuli was applied over the ulnar nerve in the wrist through surface electrodes.It was repeated every 10 seconds till loss of adduction of thumb and disappearance of T1 of TOF stimulus was noted (t2).The difference between t1 and t2 was considered as ‘ the onset time of intubation’.

Following the loss of T1 of TOF stimuli, tracheal intubation wasperformed. Condition that prevailed during intubation was recorded and was evaluated using Steyn’s modification of Helbo-Hansen scoring system. (Table 1)

Scoring scale was marked as excellent for a score of 5, good for a score of 6 to 10, poor for a score of 11 to 15 and very poor for a score of 16 to 20.

ECG, oxygen saturation and blood pressure (non-invasive) were monitored in all the patients. Data recorded include onset time of intubation, intubating conditions, heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and oxygen saturation. The above data were recorded at baseline, immediately after priming dose, immediately after intubation, and thereafter at 1 min, 2mins, at 5 mins interval till 30mins and at interval of 15mins later till the end of surgery.

Table 1 – Steyn’s modification of Helbo Hansen scoring system

Parameters	**Score**			
	1	**2**	**3**	**4**
Jaw Relaxation	Complete	Slight tone	Stiff	Rigid
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cords	Open	Moving	Closing	Closed
Coughing	None	Slight	Moderate	Severe
Limb Movement	None	Slight	Moderate	Severe

Table 2 -Comparison of onset time between the three arms of the trial

Parameter	Median (IQR)			Kruskal-Wallis Test (p value)
	A	B	C	
Onset time	145(135.5,165.6)	100(90,115)	65(55.72,82)	<0.0001

Observations and Results -

Entire data was collected and tabulated. Numerical values were represented as median for comparing the onset time of intubation for 3 different groups. Demographics profile of patients and ASA-PS were similar in all three arms of the trial.

The median onset time was 145 seconds with a inter quartile range of 135.5 seconds to 165.6 seconds in A group. With respect to B group, it was 100 seconds with inter quartile range of 90 seconds to 115 seconds and for C group the onset time was 65 seconds with inter quartile range of 55.75 seconds to 82 seconds. Between studied groups, the proportional differences in the onset time were statistically significant.

The intubating conditions were found to be excellent in all the three arms of the trial irrespective of the various priming doses.

Discussion -

Rocuronium, a Non-depolarising neuromuscular blocking agent has rapid onset of action and produces adequate muscle relaxation to help facilitates surgery and ventilation of the lung in both
elective and emergent situations. Griffth and shin, proposed that use of Priming fastens the onset time and good intubating condition by decreasing the apnoeic period during intubation[(11)]. Neuromuscular monitoring is aided in the assessing the degree of neuromuscular block during and after anaesthesia. The main complication associated with muscle relaxants is residual neuromuscular block which is overcome by TOF monitor. TOF monitor helps in identifying the degree of neuromuscular blockade effectively. This was used in our study and patients were intubated when the TOF count is 0.

The present study was a randomized controlled trial which was conducted among 75 participants, with 25 participants in each group. Group A is a control group with 0.6mg/kg of rocuronium, Group B and C are test groups ,in which

priming dose of 0.06 mg/kg and 0.10mg/kg is administered 3 minutes prior to the intubating dose of 0.54 mg/kg for Group B and 0.50mg/kg for Group C.

The onset time and intubating condition along with hemodynamic variations and adverse effects were observed intraoperatively at frequent intervals.

The distribution of age, sex between all the three groups were found to be similar. Our study results were comparable with studies done by Rao et al[6] and shashank et al.[10]

The distribution of type of surgery was found to be similar between the three groups and so is the distribution of ASA PS category between the groups. The above variables result were similar in other studies.[10][4]

The shortest onset time was observed in group C followed by group B and Group A.

The significance was very obvious indicating that priming with Rocuronium accelerated the onset time of Rocuronium's intubating dose. Priming is advantageous with regard to onset time when compared to the unprimed group. When one considers between the two groups with priming, the one that received a priming dose of 0.1 mg/Kg had earlier onset time than the one that received rocuronium priming dose of 0.06 mg/Kg. Similar results to the present study were obtained by Kumar R et al where he compared three groups but with different time intervals between the priming and intubating dose. The study suggested the time interval to be three minutes[10]. Junk KT et al also conducted a similar study by comparing Rocuronium(0.06mg/kg) and Cisatracurium(0.01mg/kg) as priming drug, respectively. The study reported that rocuronium was superior to cisatracurium in order to accelerate the intubating dose of the NMBs provided[13].

All the three groups had shown an excellent condition for intubation regardless of the various period of onset time of intubation. Similar result was obtained by Shashank et al where he compared the intubating condition obtained between rocuronium, vecuronium and cisatracurium. They concluded that all the three NMBs studied produced superior intubating condition[10]. The usage of NMBs itself with or without priming was associated with appropriate intubating condition among the study participants.

Conclusion -

The priming dose of rocuronium (0.10 mg/Kg), had accelerated the onset time of intubation compared to either normal saline or 0.06mg/kg of rocuronium in patients undergoing elective surgeries under general anaesthesia . The intubating condition produced by rocuronium was excellent irrespective of the priming technique.

Ethics approval and consent to participate–

Ethical Clearance Certificate Approval No. 636/IHEC/12-19 on 25th January, 2019 by Institutional Human Ethics Committee at Chettinad Academy of Research and Education, Chennai, Tamil Nadu, India. Informed written consent obtained.

Financial support and sponsorship–

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Availability of data statement–

The data used in this study are available and will be provided by the corresponding author on a reasonable request.

Conflicts of interest -
There are no conflicts of interest.

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